

A Policy on the Quality Use of Medicines

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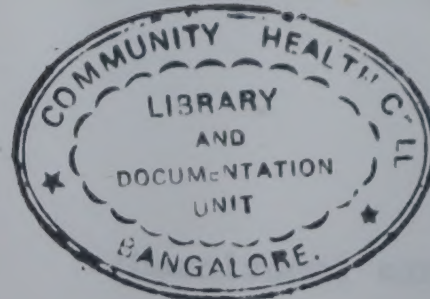
The Pharmaceutical Health and
the Rational use of Medicines
(PHARM) Committee

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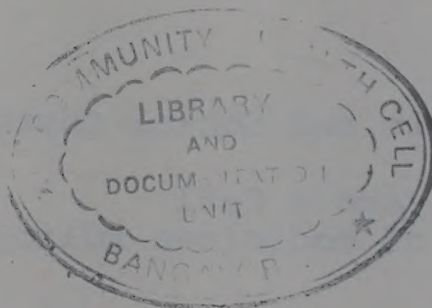


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POLICY ON THE QUALITY USE OF MEDICINES

EXECUTIVE SUMMARY

Modern medicines have transformed treatment and prevention of many diseases and have played a part in the increasing life-expectancy and improved health of Australians of all ages.

However, medicines can also cause harm. There is concern about the health, social and economic costs associated with the inappropriate use of medicines, including overuse, underuse and misuse. The challenge is to find ways of optimising the power of medicines to do good while minimising their adverse potential.

Australia has in place good systems for three important objectives relating to medicines, namely:

- . ensuring the quality, safety and efficacy of medicines;
- . providing equity of access to cost-effective medicines for all Australians; and
- . addressing issues regarding the viability of the pharmaceutical industry.

This policy deals with a crucial fourth objective, that is, the quality use of medicines. It thus provides the opportunity for Australia to formulate a comprehensive National Medicinal Drug Policy based on these four components. It anchors such a policy to good health outcomes for all Australians.

The quality with which medicines are used is influenced by the decisions and actions of many players and by a variety of structural issues affecting the environment in which these players operate. A partnership is required between consumers (including the carers of children, the aged and disabled), health professionals (especially doctors, nurses and pharmacists), government and industry. Such a partnership will identify and analyse issues and develop and implement strategies to improve the quality use of medicines in Australia.

This partnership has already been modelled by two national committees: the Pharmaceutical Health And the Rational use of Medicines (PHARM) Working Party and the Australian Pharmaceutical Advisory Council (APAC). These groups have played an important role in developing and refining this policy assisted by related government inquiries and many helpful submissions from various groups.

(b)

Appropriate and effective education of all groups, the development of innovative models of practice and the investigation of options to overcome structural and other operational constraints are the key strategies. In some areas, the need for further research will be identified as the policy is implemented.

The policy identifies the major components within which objectives and initiatives are needed. These are:

- . access to objective, relevant information by consumers and health professionals to facilitate informed decision-making. The promotion of pharmaceutical products and other sources of information should assist the aim of improving health care through the quality use of medicines (see Section 3.5a);
- . education and training of consumers (at many levels and for many target groups) and of health professionals at undergraduate, postgraduate and continuing education levels (see Section 3.5b);
- . provision of support services to practising health professionals to help solve problems in everyday practice, to develop high standards of practice, and to develop teamwork between health professionals (see Section 3.5c);
- . provision of services and resources to consumers to support them in being aware, informed and able to identify and solve problems related to medicines develop good working relationships with their health professionals (see Section 3.5d);
- . campaigns to educate the whole community about general quality use of medicines issues and problems as they arise (see Section 3.5e).

Many programs and resources have been developed by consumers, health professionals, industry and government groups over recent years. A national co-ordination and facilitation mechanism is needed to encourage further development and efficient implementation on a national basis of effective programs, resources and outcome measures. These must relate to health status, quality of life and satisfaction of the major players.

The challenge is to bring together the major players at national, regional and local levels to use their skills, resources, knowledge and experience to develop good working relationships and an environment which enables Australians to use medicines wisely and safely.

SECTION 1

INTRODUCTION

Modern medicines have transformed treatment and prevention of many diseases and have played a part in the increasing life-expectancy and improved health of Australians of all ages. However, medicines can also cause harm.

There is widespread concern over the health, social and economic costs to Australia associated with the inappropriate use of both prescribed and over-the-counter (OTC) medication. Inappropriate use refers to aspects of the marketing, distribution, prescribing, dispensing and consumption of medicines which may result in undesirable medical, social and economic consequences.

While details of the extent and nature of the issues may differ, the way medicines are used is a global concern. In 1985, the World Health Organisation called a Conference of Experts on the Rational Use of Drugs which resulted in a document known as the 'Revised Drug Strategy' (1). The 39th World Health Assembly, held in 1986, adopted this strategy which calls on governments to implement a National Medicinal Drug Policy. Australia, as a participant at this conference, was part of the development of this strategy. The need for a National Medicinal Drug Policy was further illustrated in the 'Health For All Australians' document issued jointly by all Australian Health Ministers in 1988 (2).

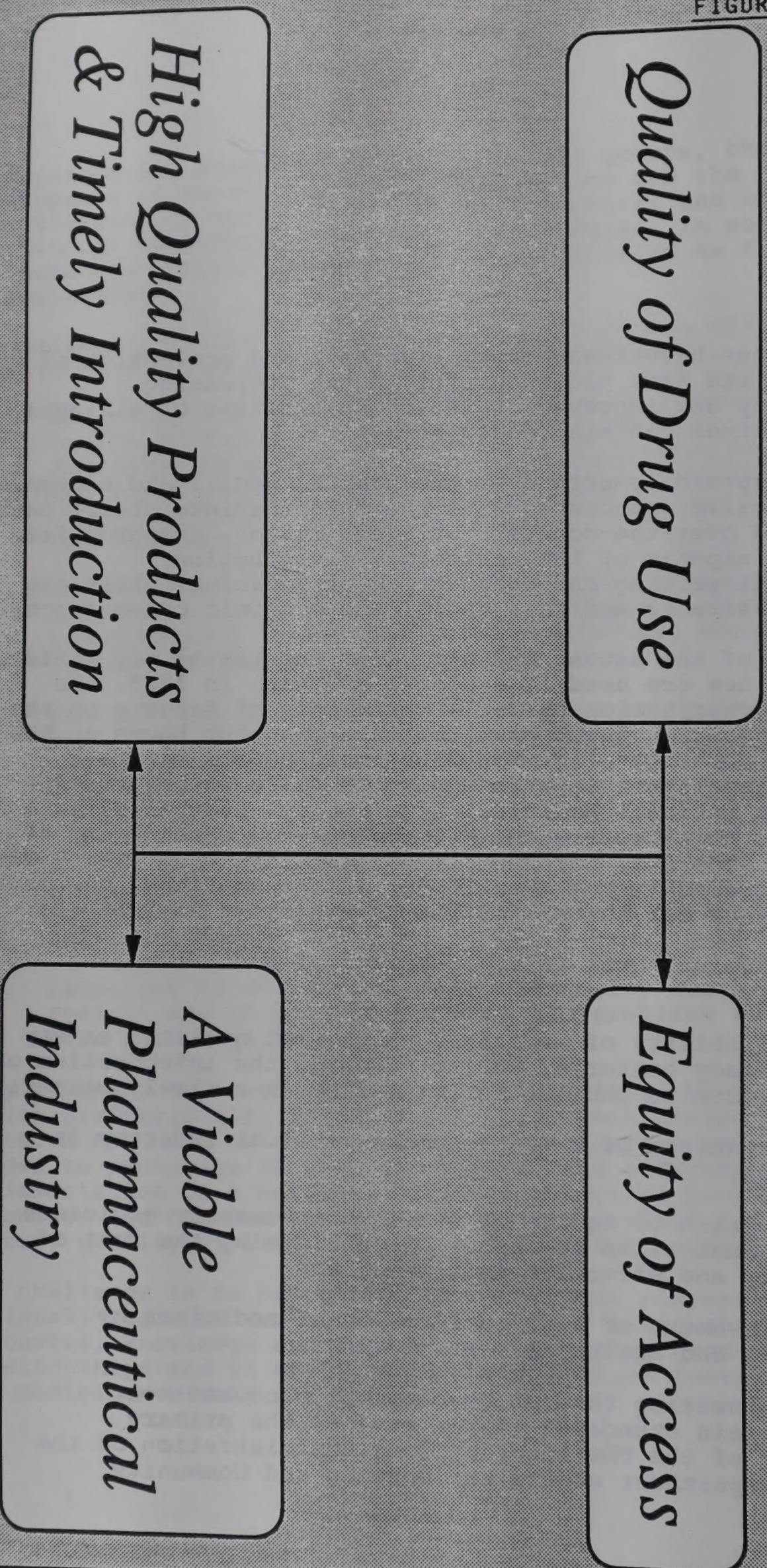
A National Medicinal Drug Policy consists of four arms (see Figure 1):

- (1) the availability of medicines which meet quality, safety and efficacy criteria, whilst allowing the introduction of new products to the Australian market in a timely manner;
- (2) the maintenance of a viable pharmaceutical industry in Australia;
- (3) the provision of equity of access to necessary medicines for the Australian community by subsidising the cost of necessary and effective medicines; and
- (4) the achievement of high quality use of medicines by consumers and health care providers.

In Australia, ensuring that pharmaceutical products meet acceptable certain standards [first arm] is the primary responsibility of the Therapeutic Goods Administration of the Commonwealth Department of Health, Housing and Community Services.

National Medicinal Drug Policy

FIGURE 1



As part of the Pharmaceutical Industry Development Program, to promote the viability of the pharmaceutical industry in Australia [second arm] the Government introduced the Factor f Scheme in 1987. The Scheme offers a financial incentive for increased domestic research and development and the export of pharmaceuticals from Australia. The Factor f Scheme is administered by the Department of Industry, Technology and Commerce. A further recent initiative aimed at promoting the viability of industry is the extension of product patent life.

Providing equity of access to medication [third arm] in Australia is the role of the Pharmaceutical Benefits Scheme, which subsidises the cost of prescription medicines of established safety and efficacy for the community.

The quality of use of medication [fourth arm] is the focus of this document. For some years, there has been a call from a variety of sources for the need for Australia to develop a policy on the quality use of medicines. This policy draws on community, professional, government and industry experience and expertise to address the broad and complex nature of the issues involved and to develop a strategy for optimising the quality use of medicines in Australia.

SECTION 2

NATURE AND EXTENT OF ISSUES IN THE QUALITY USE OF MEDICINES IN AUSTRALIA

2.1 Scope and Use of Medicines

Medicines are substances taken to prevent or to treat illness. Medicines cover a wide range of substances from herbal extracts, vitamin and mineral substances and body extracts, to chemical substances. Medicines come in a variety of forms from liquids, powders, tablets, capsules, injections, creams, ointments, inhalations, medicated bandages. The common feature of medicines is that they involve the application to, or intake into, the body of natural or synthetic chemicals. As such, medicines can be beneficial but they also can cause harmful effects to the body.

Each decision to prescribe or use medicines involves a decision which among other things should weigh the likely therapeutic benefit for that person against the risks of harm from the treatment.

No one, be it a health professional or a consumer, should become complacent about the use of medicines.

All medicines are capable of producing unwanted effects. Some adverse reactions are predictable from the medicine's pharmacological properties and others are not. Appropriate medication use may result in adverse reactions that are considered an acceptable risk.

2.2 Problems

Medicines are part of everyday life for most Australians. Medication, prescribed and/or OTC, was used by 76% of women and 65% of men at some time in the two weeks preceding the 1989-90 Australian National Health Survey. Specifically, the Survey showed that approximately 30% of the population used vitamins or minerals, 50% used analgesics, 5% used sleeping medications and 2% used tranquillisers and sedatives (3). Surveys indicate that 90% of people over 65 years of age are currently using medication (3,4).

High consumption of medication is associated with:

- . increased risk of therapeutic poisoning (5)
- . the over-prescription of some classes of medication (6)
- . sub-optimal choice of medicines within therapeutic categories by prescribers (6), and
- . the use of multiple medications by many patients (4).

Therapeutic poisoning is one aspect of the use of medicines that causes concern. Therapeutic poisoning, that is the adverse consequences of medicine excluding accidental and self-inflicted poisoning, can be divided into two categories. Firstly, preventable therapeutic poisoning, which includes such factors as inappropriate prescription or use, non-compliance and inappropriate treatment regimens. Secondly, non-preventable therapeutic poisoning which describes the occurrence of adverse effects in the course of appropriate medicine therapy. Much therapeutic poisoning occurs in the elderly and much is preventable.

In a comprehensive record linkage study conducted on poisonings by the Western Australian Health Department (5) between 1984-88, poisoning was responsible for 1.5% of all hospital admissions and 1% of all deaths. Hospitalisation was dominated by accidental poisoning in children, self-inflicted poisoning in young adults and therapeutic poisoning in the 65 years and over age group.

The standardised rate of hospitalisations due to therapeutic poisoning in Western Australia doubled between 1981 and 1988. In 1988, therapeutic poisoning caused more hospitalisations than either accidental or self-inflicted poisoning, making therapeutic poisoning the most common form of poisoning in WA. In addition, poisoning in the elderly (65 years +) more than doubled over this time (5).

A 1987 study conducted in a Melbourne teaching hospital (7) estimated that 1.6% of hospital admissions were due to therapeutic poisonings. If this pattern is indicative of the situation nation-wide, this would equate to a rate of approximately 30,000 admissions per year.

There are a number of studies which although not definitive, are nonetheless further indicators of the nature and extent of the problem.

A Fremantle hospital study found that 1% of all admissions were actually readmissions within 60 days of discharge due to non-compliance with dosage regimens. 12% of readmissions were unplanned and 16% of these were either definitely or likely to be medicine with non-compliance featuring as the main underlying cause. 14% of all readmitted patients interviewed reported taking only 75% or less of their prescribed medications. Thus, non-compliance is a considerable problem to be addressed in relation to the sub-optimal use of medicines (8).

The Victorian study referred to previously also showed that medicine interactions were responsible for 0.5% of all hospital admissions (7). However, it is important to recognise that admissions to hospital reflect only a small proportion of the therapeutic poisonings that occur in the wider community.

Medicines may be over-prescribed or prescribed in ways that are inconsistent with current management guidelines. A Drug Utilisation Sub-committee (DUSC) study of trends in antibiotic use (6) in Australia for 1987-89 has shown:

- . an over-emphasis on the use of antibiotics for the treatment of upper respiratory tract infections (URTIs) many of which are viral; and
- . that the choice of antibiotic was often inappropriate in the use of expensive broad spectrum agents.

These findings indicate prescribing that is inconsistent with recommended clinical practice (9).

A second DUSC study from the beginning of 1987 to the end of 1989 revealed that the use of lipid-lowering medications in Australia had increased from 68,120 to 304,760 prescriptions per quarter. This represents a 4.5 times increase in consumption of these medicines per head during the course of the study (10). Use was extremely high among pensioners, 45% of whom were 65 years or older. By the end of 1988, this consumption rate was 3 times that of the highest use in the Nordic countries (that is, Sweden and Norway). Further, the data suggest an inappropriate medicine selection corresponding to the relative availability of drugs and regulatory arrangements at that time under the Pharmaceutical Benefits Scheme.

A total of 10.59 million prescriptions for benzodiazepines were dispensed through Australian pharmacies in 1990, enough for 3% of the population to take a daily dose (11).

The risks associated with long term use of benzodiazepines are well documented (12). The majority of benzodiazepines (82%) prescribed within Australia were those listed on the Pharmaceutical Benefits Scheme, that is, diazepam, oxazepam, nitrazepam and temazepam. Benzodiazepine utilisation, or defined daily dose/1000 persons/day (DDD/1000/day) for 1990 was 33.73 DDD/1000/day for Australia. The defined daily dose is the average amount of drug consumed per day for the usual adult indication as defined by the World Health Organisation's Drug Utilisation Research Group.

From the Australian National Health Survey (3) it has been estimated that 330,000 Australians were using benzodiazepines daily for six months or more. The survey confirms that the major groups using benzodiazepines are women and the elderly. With the use of benzodiazepines for this duration, between 33% and 44% of patients will experience withdrawal with cessation of medication (13).

A recent study in a teaching hospital revealed that of all the patients admitted, of those taking benzodiazepines, 50% patients had done so for a period exceeding six months (14). This level of use was also confirmed in a South Australian study of residents in aged care accommodation (15).

Under-use of medication is also a matter of concern. The 1989 National Heart Foundation Risk Factor Prevalence Study found that 17% of men and 13% of women were hypertensive (that is 95 mm Hg diastolic blood pressure or more, or on medication for hypertension). As a proportion of all 'hypertensives', 47% of men and 23% of women were untreated and presumably undetected and 18% of men and 13% of women on treatment were uncontrolled. As a proportion of those on medication, 34% of men and 17% of women had a diastolic blood pressure of 95 mm Hg or more (16).

Problems have also emerged in relation to anti-asthmatic medication use (17). Reviews of prescribing of anti-asthma agents have revealed a high use of bronchodilators and a low use of preventive agents, such as disodium cromoglycate and beclomethasone. In the light of increasing concern over asthma mortality and morbidity and better knowledge about the disease process, this ratio would appear to be inappropriate.

Useful baseline data on the prevalence of asthma and thus the importance of raised community awareness and education in the management of asthma is provided by a multi-centre survey of asthma morbidity (18).

Significantly, this study of 8755 primary school children (5-12 years of age) and their parents (13,945 adults) highlighted the following:

- . the high prevalence of probable asthma in primary school children in Australia - 20.7%;
- . the reported prevalence of asthma in adults - 7%;
- . the diagnosis rate of asthma in children - 75%;
- . the under-treatment of those children with probable asthma with regular administration of the recommended prophylactic medications, that is, inhaled disodium cromoglycate and/or inhaled cortico-steroids - 25.5%;
- . the possible over-treatment with regular inhaled beta-agonist bronchodilators of children with infrequent symptoms of asthma - 40%;

the under-utilisation of the recommended tools for asthma management - peak flow meters and written action plans for severe asthma. These are used by only 6% of children with the symptoms of asthma and 7% of adults diagnosed with asthma;

optimal asthma management is improved by the diagnosis of asthma. The reported likelihood of an asthmatic having an attack severe enough to require endo-tracheal intubation or from which they will die is 10%, which again highlights the importance of optimal asthma management (19).

Another area of underuse of medicines relates to vaccines. It has been estimated that a vaccination rate of 92-96% for measles is necessary to eradicate the disease-causing organism from the community. Polio and diphtheria require 80-86% to be vaccinated, rubella requires 87%. However, Australian immunisation statistics in 1989-90 (20) show that only 89% of children aged 6 years and under are fully immunised against measles; 77% fully immunised against polio; and 81% of women have been immunised against rubella. Therefore, immunisation rates continue to be below that required to eradicate measles, polio, diphtheria and rubella from the community.

Multiple medicines use (often called polypharmacy) is also an area of concern. The use of multiple concurrent medications is not in itself inappropriate. Many patients have more than one concurrent illness and the use of multiple medications may provide significant improvements in terms of quality of life and therapeutic outcome. It must be recognised, however, that the association between reported adverse drug reactions and the number of medicines used is exponential, with a very steep increase in reported reactions with increasing number of medications (21).

The patient most at risk of an adverse drug reaction (ADR) in this situation is the elderly patient with multiple medical problems (7). Principal age-related changes in the pharmacokinetic handling of medications predisposed elderly patients to elevated concentrations of medications in the body for prolonged periods, increasing the potential for toxicity. Thus, concurrent medication intake, including non-prescription or OTC medication increases the likelihood of ADR's (22).

Furthermore, the National Health Strategy Issues Paper Number 4 identified residents of nursing homes and hostels as very high users of medicines and therefore at particular risk (23).

The Centre for Ageing Studies (4) found, in a representative sample of people aged 65 years or older, that 81% were taking at least two medications and 44% were taking at least four medicines concurrently.

Results from another recent Australian study of the use of prescribed and OTC medications in a community setting found that of the elderly population studied (N = 2805), 18% of males and 25% of females were using 3 or more therapeutic classes of prescribed medication. Of this group, 56% of males and 76% of females were also using multiple non-prescribed or OTC medication (24). What this study also demonstrates is the predictors of multiple medication use. The use of multiple prescribed medication was predicted by the following:

- . recent hospitalisation;
- . increasing age;
- . female sex; and
- . increasing depression.

However, the use of multiple non-prescribed or OTC medication was predicted only by female sex and increasing depression.

Awareness of these biological and psychosocial factors should enable the development of educational strategies for those consumers most at risk of multiple medication use and thus the increased likelihood of ADR's and highlights the need for regular review of medication in these patients.

Issues regarding the safe use of medicines, such as storage out of the reach of children to reduce the risks of childhood poisoning are still serious concerns. Childhood poisoning, defined as the ingestion of poisons (not adverse reactions to therapeutic doses of medication) is another serious concern. Poisoning accounted for 0.5% of all admissions to a major children's hospital, 66% of these were due to medication, the most common being benzodiazepines, iron preparations, paracetamol and anti-convulsants (25). Since 1956, poisoning with medicines such as these had replaced poisoning by household agents such as kerosene and pesticides (26). Over 40% of all poisoning cases presenting at public hospitals each year are the result of ingestion of pharmaceuticals (26% benzodiazepines, 9% non-opiate analgesics and 6% anti-depressants) (2). These medicines correspond to those frequently use by the community.

The issue of medicine wastage is also of concern. The WA 1987 Medi-Dump campaign encouraged consumers to take the contents of their medicine cabinets to their pharmacist for review. Of the medications returned in this campaign, 68% were obtained by prescription and 24% were OTC. The proportion totally unused was 19% (27).

Overseas studies and commentaries show the extent of the problem of adverse consequences associated with the use of medicines to be widespread. In one American survey of 239 hospital inpatients, 33% had medicine therapy-related adverse outcomes mentioned in their charts (28). In a review of 10,297 patients admitted to paediatric wards in seven British hospitals, 2% of admissions to general or speciality wards were due to adverse drug reactions (29). The elderly are at particular risk in relation to medication use (30) and adverse drug reactions severely affect the quality of life of many older patients (31). Indeed, it has been suggested that illness caused by medication may be the most significant treatable health problem among older patients (30). In the United Kingdom, the report of a comprehensive survey of medication among the elderly found inadequacies in the information elderly people were given about their medicines, in the record keeping of their doctors, in the supervision of their medication and in the care and knowledge with which medicines were sometimes prescribed (32).

In developing this policy, a major analysis and critical review of the literature on the quality use of medicines in Australia was commissioned (see Appendix I).

2.3 The Health, Economic and Social Costs

There is good Australian data outlined in Section 2.2 indicating the sub-optimal use of medicines in several areas. This is true across States, drug groups (including OTC) and population categories.

Figures do not exist which accurately represent the scale of the health, economic and social costs associated with the sub-optimal use of medicines in Australia.

Nevertheless, in an attempt to put the problem in perspective, it has been estimated that the social costs of non-compliance with medication in Australia may be as high as \$700 million a year (33). However, whilst the problem is clearly significant, this estimate is not firm as it is an extrapolation derived from several sources. The major source was a single 1979 study in a major Sydney teaching hospital of admissions due to non-compliance (estimated national cost \$532 million). Estimates were also made of the costs of hospitalisations due to: non-compliance with therapy for schizophrenia (\$41m); non compliance in the elderly (\$73m); and coronary heart disease due to non-compliance with lipid reduction (diet and medicine) therapy (\$7.5m). The study also considered the costs of asthma, diabetes and arthritis but was unable to make any firm estimates.

Even if the number of admissions due to non-compliance is half that of the estimate made in this 1979 study alone, the cost of admissions due to non-compliance would be approximately \$260 million.

There has yet to be a comprehensive and well-validated estimate made of the economic cost associated with the sub-optimal use of medicines in Australia. It is estimated that the Australian community overall spends \$2.7 billion on medication (both prescribed and OTC) per annum (34). The Commonwealth Government's Pharmaceutical Benefits Scheme (PBS), which subsidises the cost of prescription medication, costs \$1.02 billion per annum (calendar year 1991). This figure represents approximately one-eighth of the Commonwealth Government's total expenditure on health. Government subsidy of medicines through the PBS is recognised as a powerful force in keeping down the cost of pharmaceuticals.

Recent years have seen the levelling and decline in the costs associated with the PBS through the institution of a variety of policy decisions and administrative arrangements (35). These include an increase in consumer contribution through the introduction of pensioner co-payment in 1990. The impact of these arrangements on the quality of use of medicines has not been investigated to date.

There is no Australian evidence to suggest that the quality use of medicines will be achieved through cost-containment strategies alone, whether it is through consumers sharing the cost of medicines or through sensitising prescribers to their costs. Information available elsewhere shows inconclusive evidence on the overall impact of such strategies. For instance, the introduction of a limit on the number of medicines reimbursable for Medicaid patients in the American state of New Hampshire found that the policy had the unintended effect of a twofold increase in nursing home admissions (36). On the other hand, the success of a comprehensive 'value-for-money' approach in Northern Ireland has shown that significant savings can be made in the medicines bill through the promotion of a 'best buys' drugs list. These savings amounted to £34,000 per medical practice per year (37).

These concerns about the health, economic and social costs associated with sub-optimal use of medicines are wider than just in health professional circles and are indeed shared by the community at large.

2.4 Community Concerns and A Call for a Quality Use of Medicines Policy

For the community, the inappropriate use of medicines has been an ongoing concern. Sporadic calls for action took on a more articulate form by the end of the 1980s.

An area of continuing concern has been the use of benzodiazepines. Efforts in this area from 1983 have focused on the use of benzodiazepines, non-drug alternatives and other drug alternatives. These initial concerns formed the basis for campaigns designed to raise awareness among consumers (using themes such as 'Give your feelings a better chance: try to avoid tranquillisers') and/or prescribers in NSW, Victoria and Western Australia.

These were followed by other specific studies such as "Too Much of a Good Thing" (38) which examined the use and understanding of two groups of medicines by 100 older Australians. This study started to examine the nature of quality of use problems from the consumers' perspective.

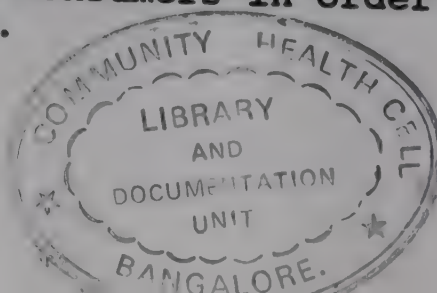
Perceived lack of progress to combat inappropriate use of medicines led the organised consumer movement to produce its own blueprint for action. In April 1989, the Consumers' Health Forum of Australia (CHF) published a document entitled "Towards a National Medicinal Drug Policy for Australia". The paper argued that, while Australia has been relatively well served in terms of ensuring quality, safety and efficacy of pharmaceutical products and in ensuring that most Australians were not denied needed medicines, the Government had failed to address the 'quality of product use' issue.

The paper also put forward the view that a National Medicinal Drug Policy would provide overall direction for all aspects of medicines and is needed to provide a framework in which the quality use of medicines can be addressed.

Under the auspices of the Australian Council on the Ageing (ACOTA), a national conference on older people and medications was held in November 1990. One of the major aims of this conference was, for the first time, to create a coalition of experts and relevant bodies to address the factors involved with the inappropriate use of medicines. This conference highlighted the significance of environmental factors such as poverty, inadequate housing and social isolation in contributing to the inappropriate use of medicines.

April 1991 saw the Consumers' Health Forum (CHF) combine with the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) to hold a two-day workshop entitled 'Rational Prescribing - The Challenge for Medical Educators' (39).

This conference examined when, what and how medical students and practising doctors should be taught about rational prescribing and indeed, how this teaching could be sustained through the prescriber's life. Another significant outcome was the special emphasis placed on the importance of good communication between health professionals and consumers in order to promote the quality use of medicines.



The social research into the medication issue by the community sector contributed to the increasing concern expressed by other groups. Health professionals themselves increasingly examined inappropriate prescribing in hospital settings and in the community (40). This widespread concern also led to the Drug Utilisation Sub-committee (DUSC) work in this area, referred to earlier in this document.

There have also been studies and recommendations made by a Joint Parliamentary Committee, by a House of Representatives Standing Committee, by the Commonwealth Department of Health, Housing and Community Services as well as numerous community organisations. In addition to this activity, there have been several inquiries and reviews conducted by different elements of Government which examined various aspects of the pharmaceutical issue (see Appendix II). The impetus for a Policy on the Quality Use of Medicines is clear.

These studies and reports have also reflected the major community concerns about perceived consumer confusion and potential for their increased exposure to risk and harm due to medicine use. Issues identified by consumers as contributing to the problem are:

- . lack of information available to consumers;
- . poor communication between consumers and health professionals;
- . cultural diversity, including poor English skills;
- . unclear labelling and inappropriate packaging of medicines;
- . environmental or structural constraints. Such constraints include the absence of non-drug alternatives in some geographical areas and the price of pharmaceuticals.

Issues identified by the other players as contributing to the problem include:

- . lack of teamwork and communication between health professionals;
- . environmental or structural constraints such as:
 - the potential for confusion and wastage arising from the split in the delivery of pharmaceutical services between public hospital pharmacies and the Pharmaceutical Benefits Scheme;
 - professional isolation;
 - time-based remuneration systems; and
 - in regard to pharmacy, remuneration for pharmacists' time in counselling.

A political response to the issues associated with the quality use of medicines was announced in the May 1988 Economic Statement where the Federal Government allocated \$2m per annum for an education program to encourage the appropriate use of prescription medication. Prescribed medication was targeted because of existing concerns over the rising cost of the Pharmaceutical Benefits Scheme (PBS). The PBS Education Program has since funded a wide variety of pharmaceutical education activities. These have included the ACOTA and CHF/ASCEPT meetings described above, as well as initiatives from consumer groups and the medical, pharmacy and nursing professions.

As alluded to earlier, the desire to do something in Australia to improve the quality of use of medicines is shared by all the major players, including prescribers (both general practitioners and specialists), nurses, pharmacists and consumers. However, the general environment in which the PBS Education Program operated was far from conducive to the promotion of the appropriate use of medication. Rather, the situation could be characterised by a lack of communication, and even animosity, between the major players.

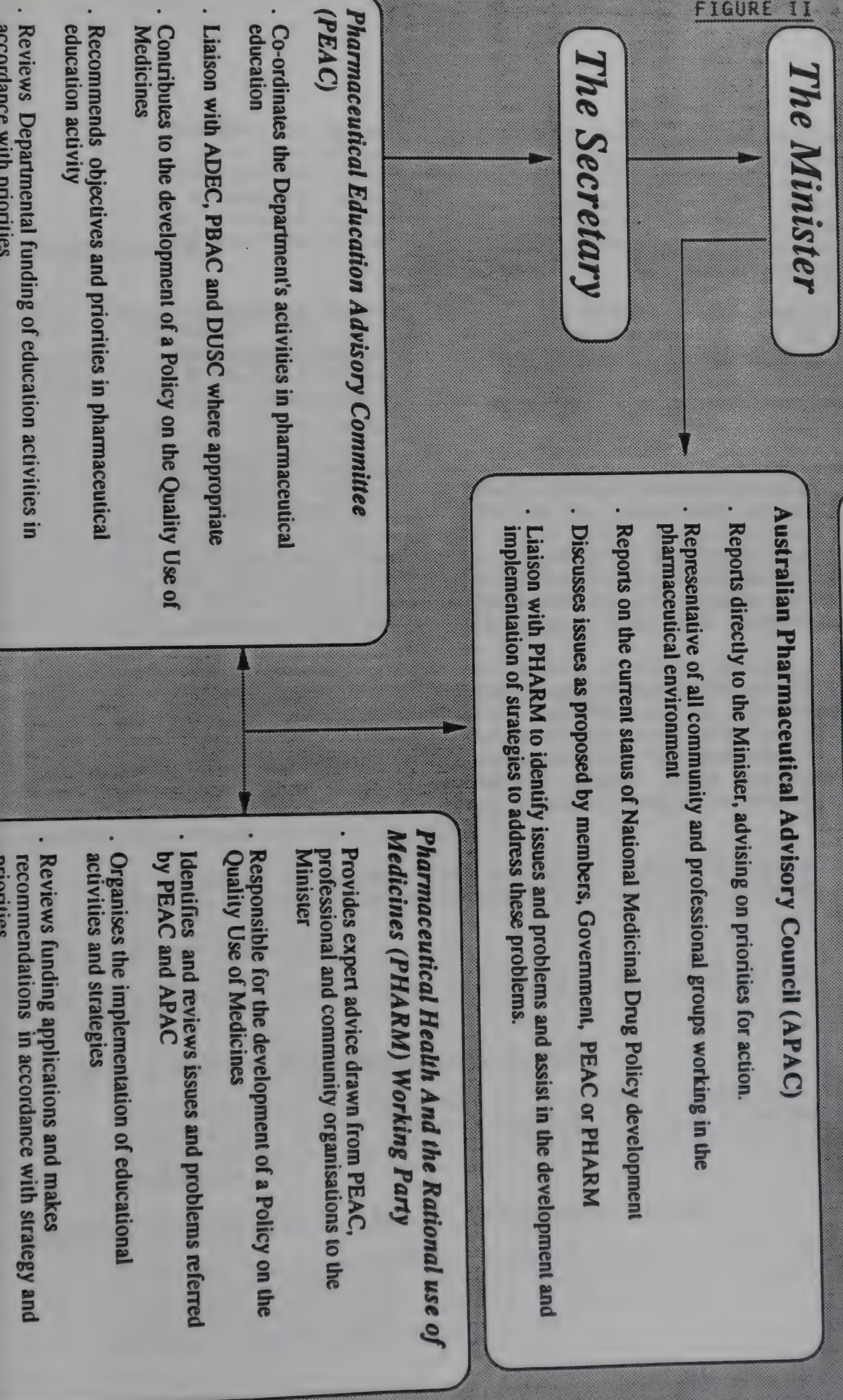
Historically, the relationship between doctors, pharmacists and other health professionals did not provide scope for open discussion of quality of use issues. A similar situation existed for the relationship between consumers and most health professionals. Indeed, each party held different perspectives on the nature of the problem and how it should be addressed.

Perhaps the most significant contribution made by the PBS Education Program was the signal it gave to these groups that the Government understood the significance of the quality use of medicines issue. Initiatives of the Commonwealth Department of Health, Housing and Community Services in the area of pharmaceutical education date back to 1988, but it was in September 1989 that the first meeting of the Pharmaceutical Education Advisory Committee (PEAC) was held.

PEAC's role is to co-ordinate the Department's activities in pharmaceutical education, across the several areas interested in promotion of quality use of medicines. Further, the Department acknowledged that in order to effect change in the pharmaceutical environment, the active participation of both professional and community groups was essential. To this end, the Pharmaceutical Health And the Rational use of Medicines (PHARM) Working Party and Australian Pharmaceutical Advisory Council (APAC) were established (see Figure II).

The Pharmaceutical Education Strategy

FIGURE 11



The establishment of these new bodies, created to address issues related to quality of use, was a key factor in changing the pharmaceutical environment. Inviting experts and the appropriate community and professional groups to have direct input to defining the issues began to move the quality of use debate from a position of confrontation to one of co-operation.

The use of medicines should be associated with substantial benefits to the community and minimal harm or cost. Benefits include reduced cost of medical care, increased life-span and quality of life, reduction in the prevalence of many serious diseases (eg. smallpox) as well as economic, social and individual advantages.

Definitive studies are required to investigate the actual contributions of medication in these areas. One important outcome must be the level of satisfaction of consumers.

The costs and problems in quality use of medicines will change or be better defined over time. There are still no comprehensive and well-validated studies which document the costs associated with the inappropriate use of medicines.

However, existing evidence shows the nature and range of the problems and validates the concerns expressed by community and professional groups, PHARM, the organisations represented on APAC and the Government. Lastly, and in contrast to the way in which quality of use issues have been addressed in the past, there now exists a fertile environment for co-operation and change in Australia.

SECTION 3

POLICY OUTLINE

3.1 What is Quality Use of Medicines?

This policy endorses the following definition of quality drug use:-

Drugs are often required for prevention, control and treatment of illness. When a drug is required, the "rational use of drugs demands that the appropriate drug be prescribed, that it be available at the right time at a price people can afford, that it be dispensed correctly, and that it be taken in the right dose at the right intervals and for the right length of time. The appropriate drug must be effective, and of acceptable quality and safety....The formulation and implementation by governments of a national drug policy are fundamental to ensure rational drug use."

World Health Organisation, 1987

3.2 Policy Goal

Recognising that many people maintain health without medicines and further recognising that medicines play a very important role in curing disease, preventing illness and maintaining health, the goal of this policy is:

to optimise medicinal drug use (both prescription and OTC) to improve health outcomes for all Australians.

3.3 Policy Objectives

The objectives of a policy on the quality use of medicines are to achieve:

Judicious selection of management options -

defining the role of drugs in treating illness and maintaining health and recognising that the management of many disorders requires the consideration of non-drug therapies;

Appropriate choice of medicine and dosage regimens -

choosing the most effective drug/s for the individual concerned taking into account their clinical condition, risk, benefit, dosage, length of treatment, cost, appropriate monitoring etc.; and



Safe use

- . minimising misuse, over-use, under-use, the ability to take appropriate actions to solve medication-related problems, eg. adverse effects, management of multiple medications etc.

3.4 Approach

3.4a The Players

In developing and implementing strategies and innovative techniques to achieve the quality use of medicines, a partnership is required between:

- . those who take or consider taking medicines;
- . those who prescribe medicines;
- . those who dispense, facilitate and monitor their use;
- . those who make, market, distribute and sell the medicines; and
- . the Government who, in the public interest, monitors safety and efficacy and provides equity of access to medicines.

Therefore the four major players are:

- . consumers and their carers, especially of the children, aged and disabled;
- . health professionals (doctors, pharmacists, nurses and others);
- . government; and
- . industry.

3.4b The Strategy

The key strategies to achieve the goals of this policy are:

- . education of all groups; and
- . the creation of an environment conducive to people making decisions and taking actions that will optimise the quality use of medicines.

Education means providing people with the tools of increased awareness, knowledge and information, skills, resources and motivation to take actions that are successful and satisfying. The creation of an environment conducive to the quality use of medicines means the identification, analysis and investigation of options to overcome structural and other operating constraints affecting the way people live and work.

A framework has been developed that allows the principles of education, behaviour change, community empowerment and social advocacy to be applied appropriately to the concept of the quality use of medicines. This framework allows strategies to be developed for each group and for combinations of programs that can be used across groups to promote more interaction.

The principles used for the development of the framework are explained in detail in Appendix III.

In addition to addressing structural issues and developing sound educational strategies, other principles are important. Groups should be encouraged to identify their needs and priorities. Programs need to involve users in their design and implementation and provide a sense of competence, ownership and participation. These programs must take account of the context and realities of people's lives. Actions taken to improve the quality use of medicines should also take into account the ethical and legal rights, obligations and responsibilities of all players, including high professional standards of practice, set and monitored by relevant peer groups.

Strategies developed must take into account the social environment and the levels of interaction at which problems arise and decisions are made. These are:

- . the individual, the inter-personal (eg. health professional-patient interaction);
- . the group, organisation and community level, (eg. consumer and professional organisations);
- . the political (eg. legislative and structural change); and
- . existing social networks.

The approach taken in the policy is that the major focus should be on consumers and health professionals who make decisions on the use of medicines and take actions daily. They should be empowered to choose and use OTC and prescribed medication well. The role of government and industry is to support health professionals and consumers in doing this. The media also has an important role to play.

3.4c A Framework for Strategy Development

The framework developed for this is called the Quality Use of Medicines Pyramid (see Figures III & IV). It is a visual representation of all the major players in a partnership.

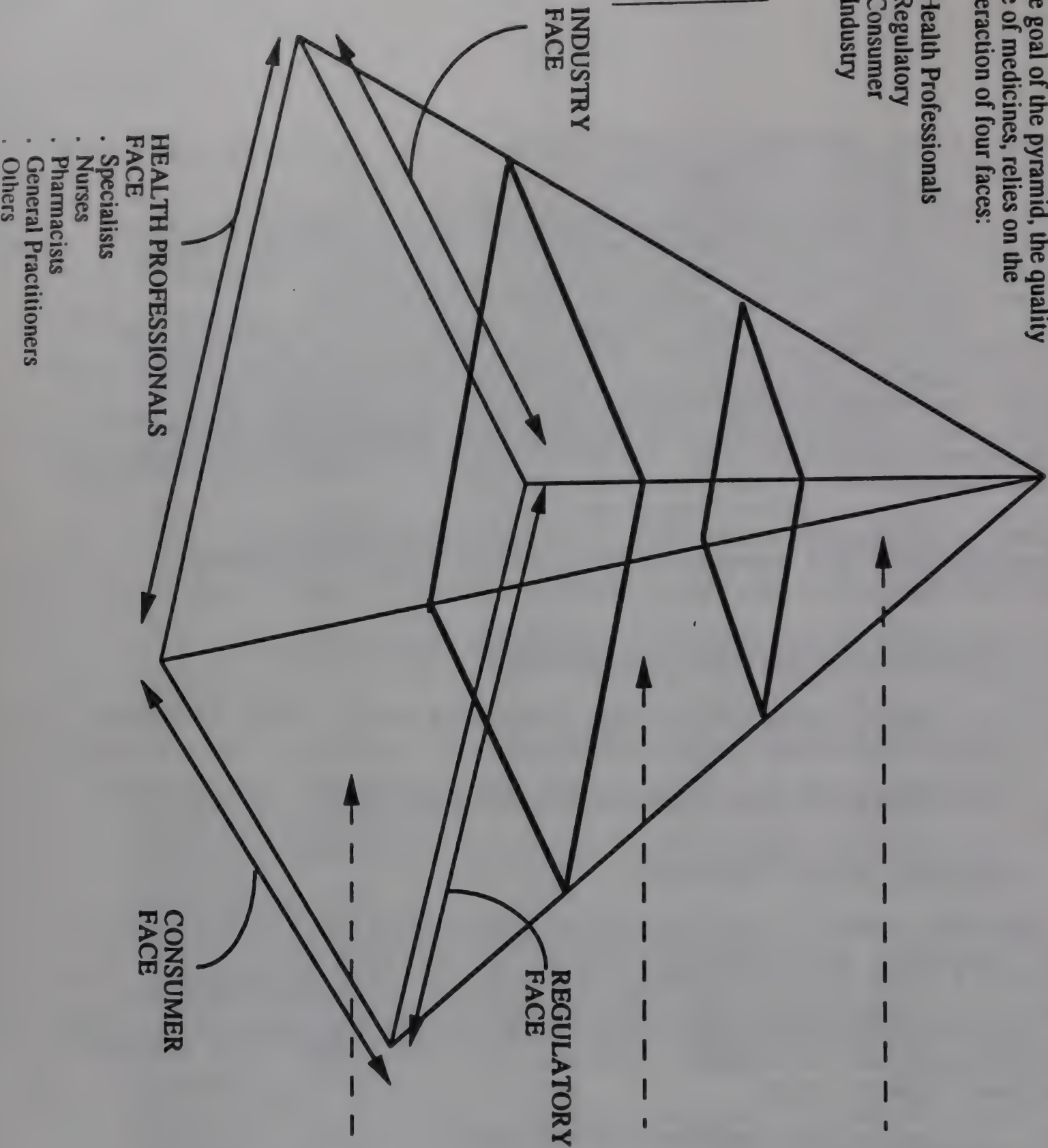
The Pyramid identifies three levels for strategy development. These levels refer to the degree of intensity of an individual's participation in quality of medicines use and apply equally to consumers and health professionals. This approach can also be applied more globally to groups and organisations such as government and industry:

The Quality Use of Medicines Pyramid

The goal of the pyramid, the quality use of medicines, relies on the interaction of four faces:

- Health Professionals
- Regulatory
- Consumer
- Industry

FIGURE III



Level 3

The Action and Evaluation Level

- > Knowledge, awareness and action needed to use medicine safely. It involves issues of monitoring positive and adverse effects, quality assurance and problem solving.

Level 2

The Knowledge and Skills Level

- > Knowledge skills and resources needed to make appropriate decisions at a personal and interpersonal level.
- > Issues important in deciding, prescribing and advising about medication in an informed way, aware of preventative options and choices for individuals.

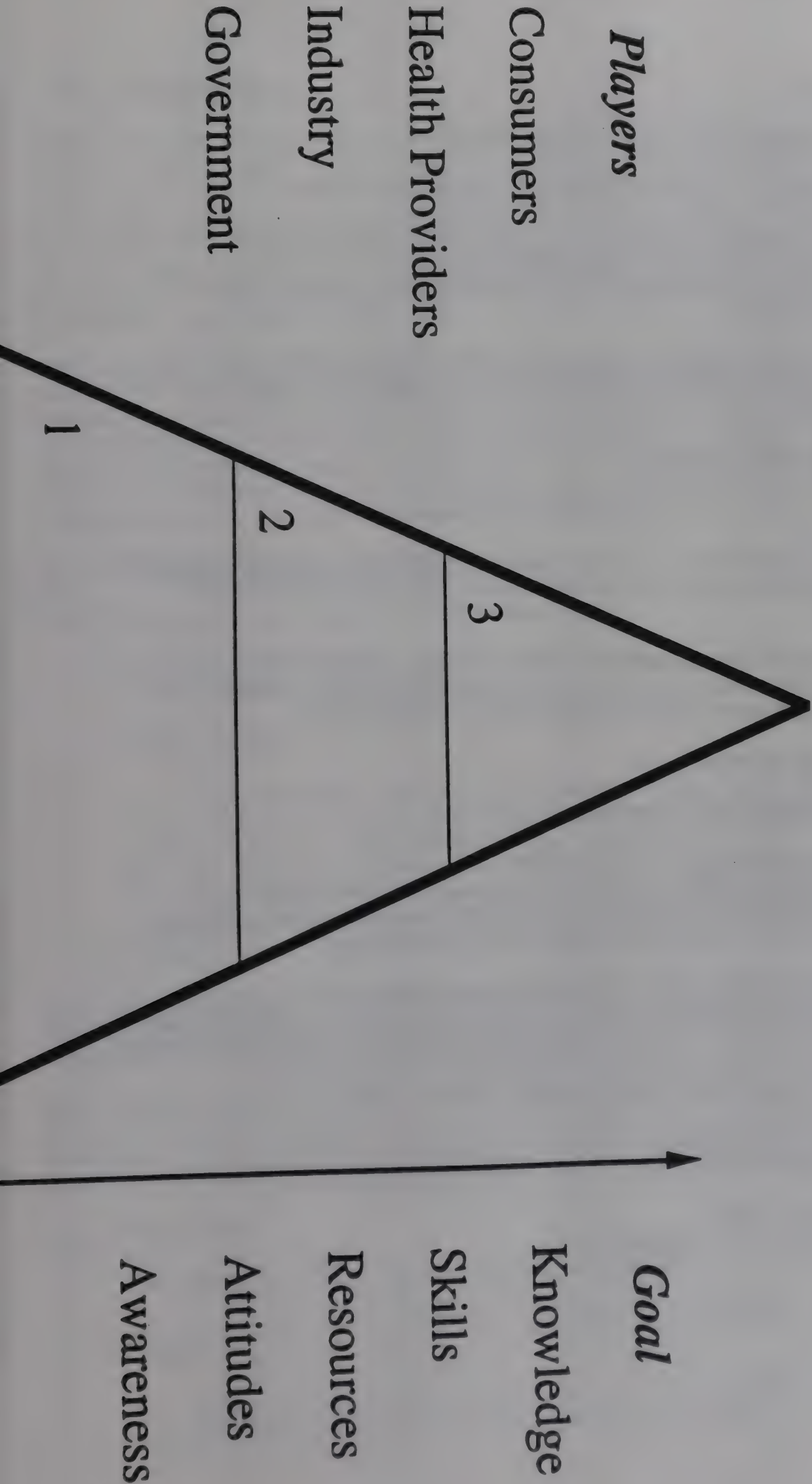
Level 1

The Awareness Level

- > Awareness of medicines as a health issue.
- > Community attitudes and beliefs about the risks and benefits associated with medicines (including those of health professionals, industry and government).
- > The goal at this level is to provide an environment conducive to optimal use of medicines, prior to any decision to prescribe or self-medicate.

Quality Use of Medicines Pyramid

FIGURE IV



Level 1: Awareness

Educational strategies at this level aim to:

- . raise awareness of medicines as a health issue;
- . explore and change community attitudes and beliefs about the risks and benefits associated with medicines (including those of health professionals, industry and government); and
- . provide an environment conducive to optimal use of medicines, prior to any decision to prescribe or self-medicate.

Level 2: Knowledge and Skills

Educational strategies at this level aim to:

- . provide the knowledge, skills and resources needed to make appropriate decisions at a personal and interpersonal level; and
- . describe issues important in deciding, prescribing and advising about medication in an informed way, aware of preventive options and choices for individuals.

Level 3: Action and Evaluation

Educational strategies at this level aim to:

- . provide the knowledge, awareness and action needed to use medicines safely. They involve issues of monitoring positive and adverse effects, quality assurance, problem solving, positive reinforcement and feedback.

The Policy on the Quality Use of Medicines requires a multi-level and multi-strategy approach, especially given that not all people will have the desire, motivation or need to work through all levels of the pyramid. Further, the Policy recognises that educational strategies need to be:

- . of reasonable duration;
- . provide co-ordinated and consistent messages;
- . adaptable;
- . research-based; and
- . have an evaluation component.

3.4d Partnership

Each of the major players has a role in promoting the quality use of medicines. The need for consultation between each of the major players (consumers, health professionals, government and industry) concerning the nature of the problem, the definition of terms and the need for action in response to problems that arise from time to time is very important. In this regard, the primacy of the relationship between the prescriber and the consumer is acknowledged.

The pyramid shows graphically the great need for groups to work together. The aim of this policy is to stimulate links, communication and cross-fertilisation between the players. This is especially important given the potential impact of this policy on other areas of Australia's National Medicinal Drug Policy. Recognition of this fact was reflected in the establishment of the PHARM Working Party.

3.4e Policy Goals for Each Player

For Consumers and Health Professionals:

- . to make consumers and health professionals more aware of the risks and benefits of medicines, the possibility of non-drug alternatives and the importance of a healthy life-style;
- . to give people the information, skills and resources to make decisions and take actions that enable the wise use and choice of medicines when required; and
- . to help people develop skills and confidence to use medicines safely and seek help to solve problems when they arise.

The quality use of medicines will enable consumers to be more self-reliant and knowledgeable, and maximise the health benefits associated with the use of medication.

For health professionals, the quality use of medicines should provide the skills and support required to achieve better health outcomes for patients, thereby increasing job satisfaction and making the health professionals' work easier.

For Government:

- . to develop and implement this policy ;
- . to co-ordinate existing relevant Government programs; and
- . to investigate the structural and environmental issues which affect the quality use of medicines.

This policy will enable Government to place the quality use of medicines in the broader context of health policy development and the range of other services the Government provides, drug evaluation, the Pharmaceutical Benefits Scheme, health promotion programs etc.

For Industry:

- . to encourage industry to continue the development of safe and effective products to cure illness and maintain health;
- . to market and promote their pharmaceutical products in a manner that facilitates quality of use;
- . to encourage industry to provide good quality information and education services that are conducive to promoting the quality use of medicines; and
- . to discourage information and education activities that are not conducive to the good quality use of medicines.

For industry, this policy encourages the quality use of quality products.

3.5 Major Strategic Policy Components

In developing strategies, this policy has tried to identify approaches that will:

- . empower consumers to use medicine well;
- . empower health professional (doctors, pharmacists, nurses, others) to help consumers use medicine well;
- . define what constitutes effective education;
- . define what combination of information, skills and motivation will be effective for different groups in Australian society;
- . define the standards that should apply and who should set them; and
- . work in practice.

Five key areas have been identified for the development and provision of basic prerequisites for facilitating the quality use of medicines (Figure V illustrates these components and Figure VI gives some examples of initiatives in each area). These are:

- . the provision of objective information and the ethical promotion of medicines;
- . the facilitation of good training for quality use of medicines;
- . the provision of important consumer services;

Policy on Quality Use of Medicines

Major Components

FIGURE V

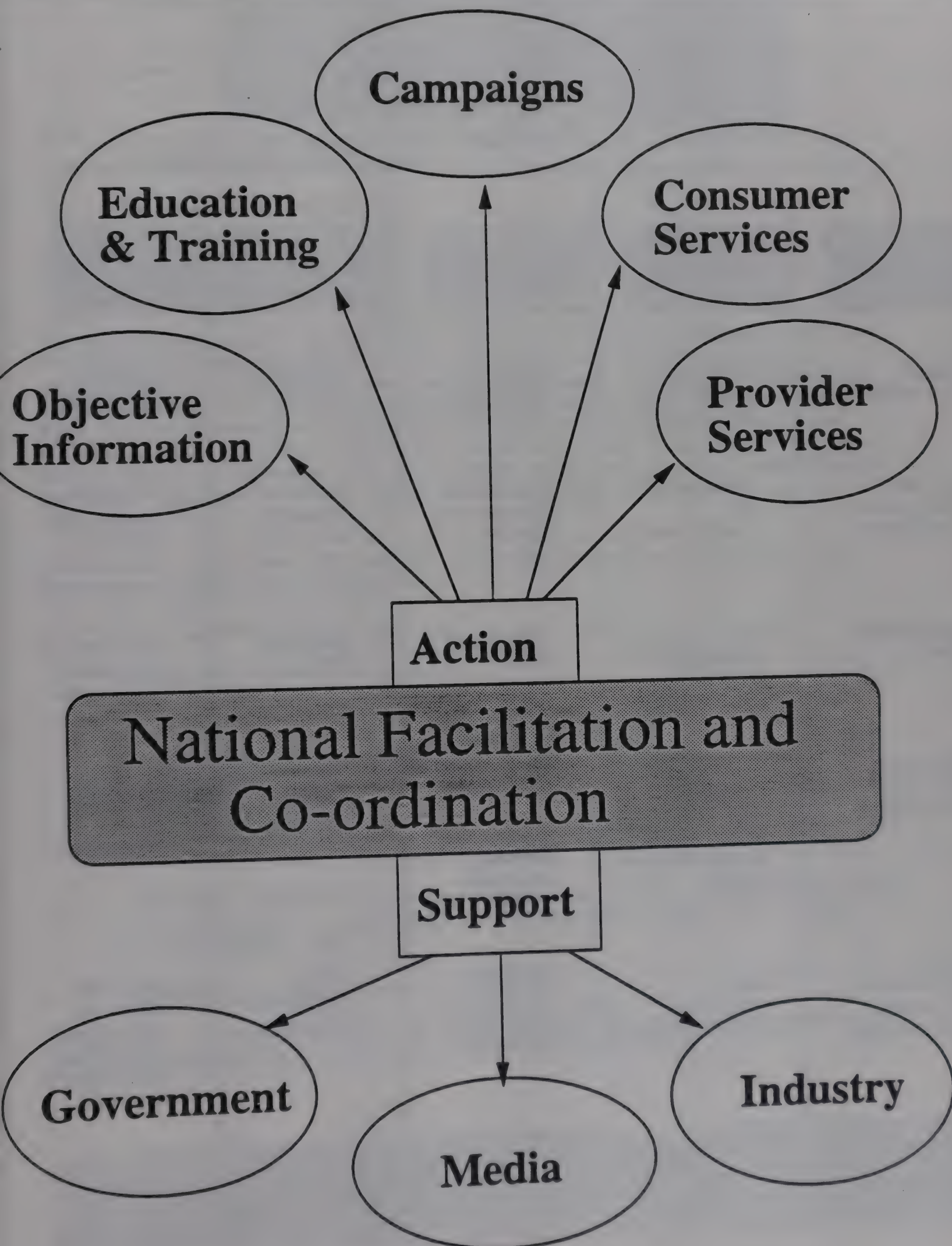
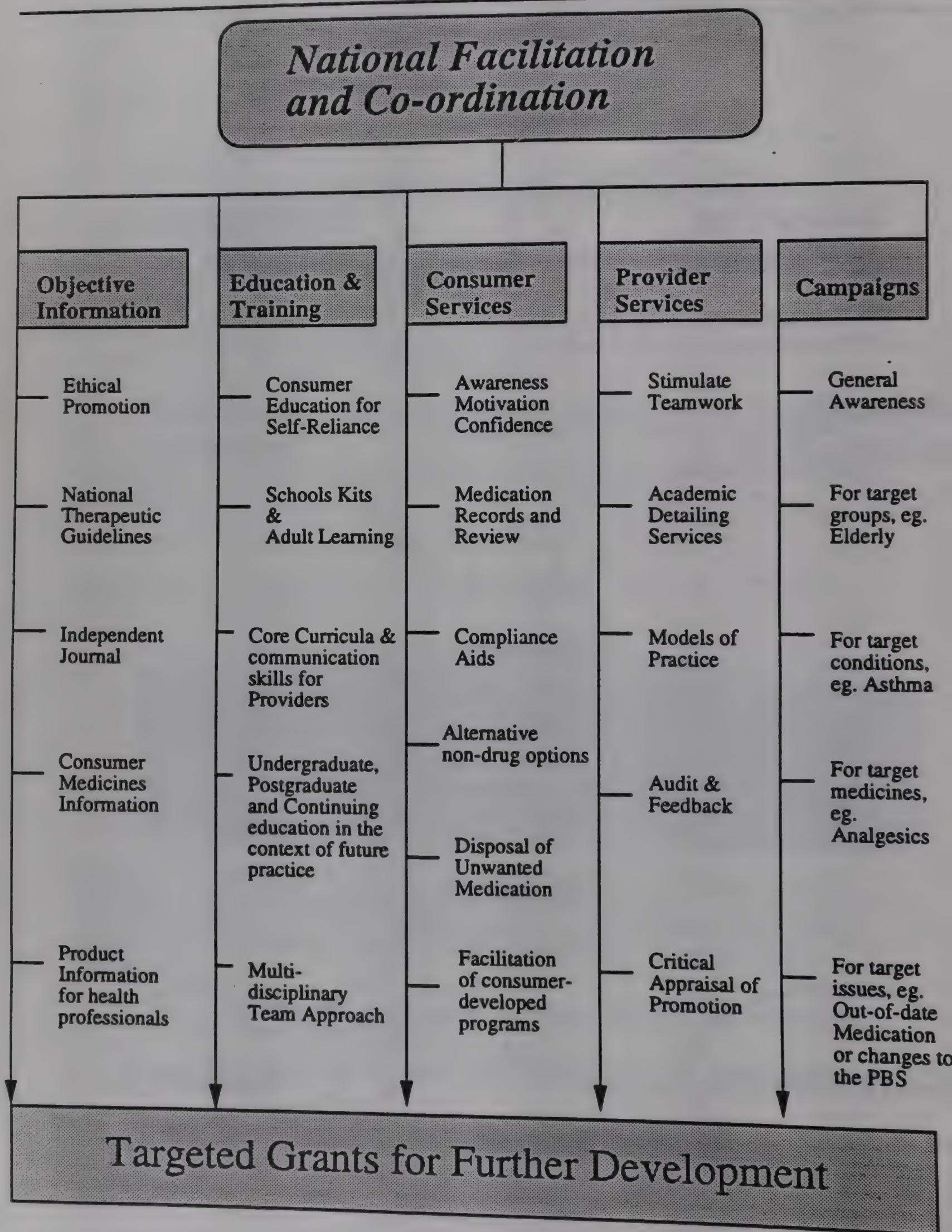


FIGURE VI



- . the provision of important services to health professionals; and
- . regular educative campaigns targeting general or specific issues that are raised in relation to use of medicines.

3.5a Provision of Objective Information and the Ethical Promotion of Medicines

i. Objective Information

Objective information is needed by consumers and health professionals to provide basic high quality data and facilitate informed decision-making.

An important issue in relation to objective information is the difference between product information and guidance for prescribing. The dissemination of approved product information is important in informing prescribers about the way to use particular products. Guidance for prescribing considers the relative merits of a particular medicine and its role in the management of disease. This is much more an area of considered opinion and needs to be seen to be independent and authoritative.

Consumers also need access to information about products and treatment options available.

All this information should be:

- . based on agreed standards;
- . available, accessible and understandable by users;
- . flexible and provided in a variety of forms suitable for users;
- . independently sourced with no advertising associated with it;
- . relevant to the wants and needs of users, especially those of aboriginal, non-English speaking and varying ethnic backgrounds; and
- . ethically promoted.

It should preferably include user groups in its development and be pilot-tested for usefulness and acceptability.

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ii. Ethical Promotion of Medicines

This policy endorses the ethical criteria for medicinal drug promotion developed by World Health Organisation, which urges each country to:

"...develop their own appropriate measures to ensure medicinal drug promotion supports the aim of improving health care through the rational use of drugs" (41).

In this country, the task of ensuring that industry advertises and promotes its products in an ethical manner is the responsibility of the industry itself through self-regulation.

The Trade Practices Commission in a recent review (42) found that reasonable standards have been achieved in relation to self-regulation of promotion by both the Australian Pharmaceutical Manufacturers' Association and the Proprietary Medicines Association of Australia.

It noted that, while the industry self-regulatory system had been effective in reducing the problem of misleading advertisements, there was still room for further improvement. The TPC made a number of recommendations to achieve this goal, including independent audit and monitoring of pharmaceutical promotion.

This policy supports the principle that health professionals and consumers should be educated to adopt a critical approach to all types of information about medicines and non-drug alternatives, including pharmaceutical promotion and other sources of information and should be encouraged to participate in the monitoring process.

3.5b Education and Training

Appropriate training provides the prerequisites of knowledge, skills and awareness for quality use of medicines for all groups. This education should occur within a quality use of medicines framework which allows discussion of the role of medicines in health.

The aims are:

- to stimulate the development of education about health and the role medicines play in maintaining and restoring health at primary school and high school levels and in many different forums of adult education. The participation of health care workers in these situations should be considered;

to ensure adequate emphasis on communication skills as part of the undergraduate and post-graduate training of health professionals. These skills include:

- listening
- non-judgemental attitude
- verbal and non-verbal communication
- use of non-technical language
- patient education
- special skills for particular groups, such as the elderly, people from non-English speaking backgrounds, the intellectually disabled etc.
- supportive written take-home information providing specific instructions.

to develop good quality curricula in clinical pharmacology and therapeutics, and the teaching of quality use of medicines skills in the context in which they will be used for general practitioners, pharmacists and nurses. Integral to this is the overall promotion of the relevant speciality of clinical pharmacology including expanding training and career opportunities;

to encourage hospital-based training of health professionals to provide the skills and orientation relevant to later community practice. This could be achieved by the formation of hospital-based quality use of medicines committees comprising both hospital and community-based health professionals and consumers;

to teach critical appraisal skills for assessing information provided by drug companies or other sources; and

to ensure that the best of these are available at under-graduate, post-graduate and continuing education levels and to encourage a multi-disciplinary team approach right from under-graduate education between these three professional groups.

3.5c Consumer Services

The aim is to support and stimulate the development of a variety of programs that help consumers to become:

- more aware about medicines and their benefits and risks;
- more motivated and confident to ask for more information from health professionals or to seek it from appropriate sources; and

- . more confident and able to ask for help to solve problems that arise during drug therapy and more aware and encouraged to take preventive action such as asking for periodic medication review and disposing of out-of-date medication.

Resources to help consumers in this area, such as medication records and compliance aids, should be evaluated and/or developed as appropriate.

3.5d Provider Services

The aim is to develop and deliver services to help providers:

- . to use objective information and other services to solve practical prescribing problems they encounter in practice;
- . to develop more knowledge and skills to improve the quality of their practice;
- . to use academic detailing and other methods (such as national therapeutic guidelines) which assist them in developing their professional standards;
- . to become interested in self-audit about prescribing and dispensing practice;
- . to stimulate more teamwork in everyday practice between health professionals and to help professionals develop skills to more critically appraise information they receive from drug companies and other sources; and
- . to develop different models of practice and better integrate the services provided by all health professionals.

3.5e National Educative Campaigns

There is an on-going need for both general awareness campaigns and those that target specific problem areas identified by the Drug Utilisation Sub-committee (DUSC), professional/consumer groups, or by research carried out by various bodies. The focus of such campaigns might be the elderly, or a disease condition such as asthma, or a particular drug group such as analgesics or particular situations such as medicine use in nursing homes.

3.6 National Co-ordination and Facilitation

Activities within the five areas identified above (3.5a to 3.5e) need to occur at many levels.

Some important initiatives to promote the quality use of medicines in Australia are already being undertaken. Examples are the production of an independent journal, the preparation of prescribing guidelines, the development of consumer education materials and the conduct of academic detailing programs. Other activities such as services to health professionals and consumers, and national educative campaigns need to be facilitated or developed.

The quality use of medicines is predicated on the close involvement of groups which set professional standards of practice and understand the needs and concerns of community groups. A strong principle underlying the approach to optimising the use of medicines is to stimulate and support initiatives within local communities or professional and consumer groups and to support existing groups already developing initiatives wherever possible rather than 'reinventing the wheel'.

A mechanism is therefore needed that facilitates, co-ordinates and supports initiatives at State, regional and local levels in a way that honours this principle. This co-ordinating mechanism will operate most effectively by being set up outside government.

In this respect, the quality of use arm of the National Medicinal Drug Policy is different to the other arms, which sit well within government; i.e. the Therapeutic Goods Administration, Pharmaceutical Benefits Scheme in the Commonwealth Department of Health, Housing and Community Services and the 'Factor f' program within the Commonwealth Department of Industry, Technology and Commerce.

3.7 Relationship to the Commonwealth Department of Health, Housing and Community Services and the Other Arms of the National Medicinal Drug Policy

There is a need for a corresponding section or branch within the Department that develops policy in the quality use of medicines area. It is vital also that there exist a mechanism for the four arms of the National Medicinal Drug Policy to come together at a senior level within government. This level of co-operation is necessary to ensure that the objectives of each arm are met without adversely affecting outcomes in other arms.

The overall impact of actions in all arms on meeting the objectives of the National Medicinal Drug Policy as a whole, need to be assessed by such a mechanism.

There are many issues that require discussion and debate. In some cases it is important that the four arms are able to stay separate and provide a commentary on the effects of decisions in one area on the issues in another. However, in many cases a combined approach working in partnership between arms of the national drug policy will be required.

For example, the process in Therapeutic Goods Administration whereby the development of objective and evaluated product information and patient information is developed is of vital concern to quality use of medicines. However, the wealth of other important information developed by different groups outside the industry/government regulatory process demands a mechanism for ensuring that it meets appropriate quality of use standards.

In the Pharmaceutical Benefits area, it is important that combined approaches of regulation and education be developed to respond to certain situations. There are several examples that could illustrate this. One concerning the H₂ receptor antagonists is given in Appendix IV. Another example concerns analgesic use in the community. The relative effectiveness of scheduling to limit consumer access versus review of marketing approval for ineffective or inappropriate indications, versus education to encourage appropriate and safe use for consumers has been debated. Some combined approach using all three strategies might produce a more powerful result that decreases risk and harm and increases appropriate and safe use.

In addressing issues concerning the viability of the pharmaceutical industry, debate should occur between, on the one hand issues affecting the economic welfare of Australia addressed by the 'Factor f' program, and on the other hand issues affecting the health of Australia addressed by the other three arms of a National Medicinal Drug Policy. Policy decisions should reflect balanced consideration of both the health and economic perspectives.

The continued existence of a body such as APAC in providing direct advice to the Minister from representative groups in the community is important for two reasons. The first is that such a body serves to identify and seek solutions to issues of concern to various community, professional and industry groups. Secondly, it is an important conduit by which to gain the support of these groups for initiatives that respond to these concerns.

3.8 Evaluation

3.8a Quality Use of Medicines Outcomes

Deciding on which indicators of the quality use of medicines are appropriate and how they should be measured and interpreted is the task of the policy co-ordinating mechanism (see Section 3.6).

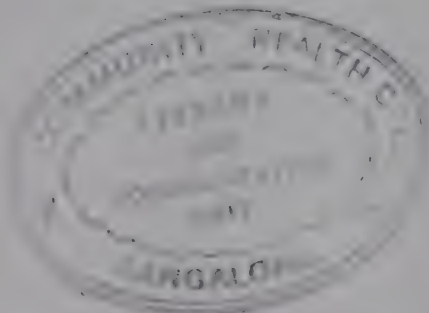
The formulation of outcome measures should necessarily involve the relevant groups as these indicators must be acceptable to those groups whose actions are being interpreted. For example, outcome indicators are not, by definition, standards. The process of setting standards must involve the groups to which they will apply, obtaining their agreement that such standards are both desirable and achievable. It is also vital that this same process calls for such standards to be used appropriately in making judgements about actions.

Deviation from the norm, whether in terms of average cost or average volume of prescribing, cannot be an acceptable basis for judging the appropriateness or quality of prescribing. The norm really describes current practice, and may reflect 'good' or 'poor' quality prescribing. For this reason, setting standards in terms of percentage of prescriptions written will not necessarily be acceptable. A knowledge of the context and frequency of clinical problems presenting to the physician concerned is needed before appropriate judgements can be made. These judgements are best made by the prescriber's peers.

The way Health Insurance Commission (HIC) data is used and interpreted in this sense is extremely important and a sensitive issue in the medical community. All agree that fraud is wrong and should be detected and penalised, and these are clearly the tasks of the HIC. Further, as an information service, the feedback of HIC data on prescribing to individual doctors is likely to be welcomed by them. However, the interpretation of this data and judgement about the appropriateness of prescribing requires peer expert knowledge of the practice profile and the pattern of clinical problems presenting to the prescriber.

3.8b Data Sets and Indicators

The important data sets that have been identified for quality use of medicines outcomes are outlined below:



i. Health Indicators

- A. The Australian National Health Survey (ANHS) carried out by the Bureau of Statistics provides:
- . information on the extent of medication use by the whole Australian population;
 - . information on the use of health services in general and for certain specified conditions.

Therefore, some broad conclusions can be drawn about the usage of medicines and health consequences.

The survey is carried out every five years. It is important for monitoring the quality use of medicines that this survey continues to collect data on medication usage. A quality use of medicines co-ordinating mechanism should increasingly provide input to the scope and type of questions asked about medicines.

B. National Morbidity and Prescribing Surveys:

These surveys of general practice link indications with management decisions, in particular, prescribing. Some judgement of the appropriateness of prescribing can thus be made.

There are two approaches currently available:

- . ongoing surveys provided by market research companies such as IMS and Walsh International;
- . occasional morbidity surveys; the Family Medicine Research Unit at the University of Sydney has developed the methodology and is responsible for the recently completed survey.

The quality use of medicines co-ordinating mechanism (and DUSC) should negotiate the purchase of market research and sales data on a regular basis for specific purposes related to assessing the quality of use of medicines.

The morbidity surveys need to be carried out regularly, perhaps every five years.

C. Hospital Admissions Casemix Program:

This program could provide data on admissions for various diagnoses, for example, therapeutic poisoning.

ii. National Data on Dispensing

The best database is that of the Drug Utilisation Subcommittee (DUSC) of the Pharmaceutical Benefits Advisory Committee. It now provides data based on dispensing by community pharmacists of prescription medicines. It allows trends and levels of dispensing to be monitored and allows identification of potential problems in the use of medicines. This data set needs to be supported, maintained and expanded to include, if possible, hospital dispensing for which there is currently no national data base.

iii. Social Indicators

Methods of measuring social indicators relevant to quality use of medicines issues need to be developed and updated regularly.

Examples of these are:

- perceptions of the major consumer, professional, industry and government groups, as well as those of community-based organisations with a specific health focus, for example, Diabetes Australia, the Arthritis Foundation:

- awareness;
- knowledge;
- access to information;
- skills;
- use of resources;
- actions taken to solve medication-related problems;
- satisfaction; and
- perception of problems.

iv. Cost

The cost of medication to the community either through the PBS or overall should be monitored. Means of measuring the cost of poor quality use of medicines and its impact on health outcomes should be developed. Any impact resulting from changes to the PBS, on either equity of access or the quality use of medicines, also needs to be monitored.

3.8c The Need for Further Studies

A variety of indicators need to be measured in order to give a composite picture of how the major objectives of this policy are being achieved. Focused studies are needed on issues such as admission rates for therapeutic poisoning and also on wastage, especially of unused medicines.

These studies need to be carried out at local, regional and State levels. There is some evidence of the nature and extent of morbidity due to inappropriate medicine use in health care institutions but very little in the community.

The quality use of medicines should yield substantial benefits not only in health care institutions but also in the wider community through better health outcomes, better medicine use, increased national productivity and quality of life. It will be on these end points that the success of the policy will be judged.

SECTION 4

CONCLUSION

The proposed policy on the quality use of medicines will produce better health outcomes for Australians in several ways.

Firstly, the recommendations made in the proposed policy will contribute significantly to the ability of the four arms of a National Medicinal Drug Policy to work together. The Pharmaceutical Benefits Scheme (PBS) is acknowledged as one of the most equitable schemes in the world. This policy will encourage Australians to use the PBS as well as possible.

It will also result in the development of agreed performance indicators by which both the quality of use of medicines and the cost-effectiveness of the PBS can be assessed. Such indicators must include increasing the judicious selection of management options, increasing the appropriate choice of medicines and dosage regimens, and increasing the safe use of medicines.

Further, the proposed policy indicates the means by which Australia's high standards of manufacture and testing are not undermined by inappropriate use.

Neighbouring countries are also developing national medicinal drug policies in which quality of use is an important consideration. The educational expertise, methodology and products developed by this policy will themselves be exportable. Also, the implementation of this policy will firmly establish Australia as a major player in this important area, both within our region, and within the larger membership of the World Health Organisation.

Another major benefit to Australia offered by this policy is that it offers a mechanism whereby key short and long-term educational initiatives can be put in place.

These initiatives will:

- make consumers and health professionals more aware, informed, skilful and motivated to use medicines well, in combination with healthy life-styles; and
- create strong links and co-operation between health professionals themselves, and between them and consumers. Thus, when particular problems are identified, a strategy and action plan can be quickly developed.

Through the implementation of this policy, the quality use of medicines will yield substantial benefits not only in health care institutions but also in the wider community through better health outcomes, better medicine use, increased national productivity and quality of life. It will be on these end points that the success of the policy will be judged.

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REFERENCES

1. World Health Assembly, 'Revised Drug Strategy', May 1986, p. 93.
2. Health Targets and Implementation (Health For All) Committee, 'Health for All Australians', Canberra, 1988, pp. 63-4.
3. 'Australian National Health Survey 1989-90', Australian Bureau of Statistics, Canberra, 1991.
4. 'The Australian Longitudinal Study of Ageing: Key Findings of a Multidimensional Pilot Survey', Centre for Ageing Studies, Adelaide, 1990.
5. Waddell VP, Serafino, S; 'An Analysis of Hospital Morbidity and Mortality due to Accidental and Self-inflicted Poisonings', 'Poisoning in Western Australia 1984-1988', Statistical Series/25, Health Department of Western Australia, Perth 1991.
6. Birkett, DJ et al; 'Profiles of antibacterial use in Australia and trends from 1987 to 1989: A report from the Drug Utilisation Subcommittee of the Pharmaceutical Benefits Advisory Committee', 'Medical Journal of Australia', Vol. 155, pp. 410-415, September 16, 1991.
7. Larmour I, Dolphin R et al; 'A Prospective Study of Hospital Admissions due to Drug Reactions', 'Australian Journal of Hospital Pharmacy', Vol. 21, No.2, 1991, pp. 90-95.
8. 'Readmissions to Fremantle Hospital (Parts 1 and 2)', 'Fremantle Hospital Drug Bulletin', May, June and October 1991, Fremantle.
9. Antibiotics Guidelines Subcommittee of the Victorian Drug Usage Advisory Committee, 'Antibiotics Guidelines', 6th edition, Toorak Victorian Medical Postgraduate Foundation, 1990.
10. Henry, DA et al Recent trends in the prescribing of cholesterol lowering drugs in Australia: A report from the Drug Utilisation Subcommittee of the Pharmaceutical Benefits Advisory Committee, 'Medical Journal of Australia', Vol 155, pp. 332-336, September 2, 1991.

References (cont.)

11. Mant A et al, 'Benzodiazepine Utilisation in Australia with International Comparisons', Medical Journal of Australia, Canberra, 1992 (in press). For copies, contact the Drug Utilisation Sub-committee (Secretary), Department of Health, Housing of Community Services, GPO Box 9848, Canberra, ACT, 2601.
12. Lockwood A, Berbatis C G; 'Benzodiazepine Drugs in Australia: Associated Mortality and Morbidity', Drug and Alcohol Review 1990, 3, pp. 277-287.
13. Tyrer P, 'Dependence as a Limiting Factor in the Clinical Use of Minor Tranquillisers' Psychotropic Drugs of Abuse, International Encyclopaedia of Pharmacology and Therapeutics, Chapter 7, New York, 1990.
14. Carey D, Day R O et al; 'An Attempt to Influence Hypnotic and Sedative Drug Use', Medical Journal of Australia, Vol 156, March 16, 1992, pp. 389-396.
15. Gilbert A, Quintrell L & Owen N, 'Trends over Six Years in Benzodiazepine Use among Residents of Aged Care Accommodation', Journal of Social and Administrative Pharmacy, 7, 1990, pp. 123- 129.
16. Risk Factor Prevalence Study, National Heart Foundation, Canberra, 1989.
17. Woolcock AJ, Jenkins C R; 'Management of asthma: a decreasing role for bronchodilators', Modern Medicine, 34, 1991, p.18.
18. Bauman A, Mitchell A, et al, 'Asthma Morbidity in Australia: An Epidemiological Study', Medical Journal of Australia, 156, 1992, p. 827.
19. Olsen LG, Saul P, 'Management of Life Threatening Asthma in Isolated Practice', Current Therapeutics, June 1992, p. 47.
20. Australia's Health 1992, AGPS, Canberra, 1992, p.75.
21. Williamson J, Chopin J, 'Adverse Reactions to Prescribed Drugs, A Multicentre Investigation', Age Ageing, 1980, 9, pp. 73-80.
22. Mant A, Whicker S et al, 'Over-the-Counter Self Medication', Drugs and Ageing Journal, Vol. 4, 1992, p. 257.
23. National Health Strategy Issues Paper No. 4, June 1992, p. 25.

References (cont.)

24. Simons LA, Tett S et al, 'Multiple Medication Use in the Elderly of Prescription and Non-Prescription Drugs in an Australian Community Setting', Medical Journal of Australia, 1992, 157, p. 242.
25. Campbell D, Oates R K, 'Childhood Poisoning - A Changing Profile with Scope for Prevention', Medical Journal of Australia, 156, p 238, 1992.
26. Beveridge J, 'Accidental Poisoning in Childhood', Medical Journal of Australia, 1, p 216, 1956.
27. Longmore R, McDonald C, Sunderland B, et al; 'Examination of a Sample from a MediDump Campaigning in Perth, Western Australia', Australian Pharmacist, 1990, 9, p 145.
28. Koelchler J et al., 'Indicators for the Selection of Ambulatory Patients who warrant Pharmacist Monitoring', American Journal of Hospital Pharmacy, 1989, 46: pp. 729-732.
29. Mitchell A, Lacouture P et al, 'Adverse Drug Reaction in Children Leading to Hospital Admission', Paediatrics, 1988, Vol 82, pp. 24-29.
30. Beers M, Ouslander J, 'Risk Factors in Geriatric Drug Prescribing', Current Therapeutics, March 1989, pp. 107-120.
31. Fink A et al, 'Assuring the Quality of Health Care for Older Persons', Journal of the American Medical Association, 1987, 258, pp. 1905-1908,
32. Cartwright A, Smith C, Elderly People, Their Medicines and Their Doctors, Routledge, London, 1988.
33. Plant A, Gross P; 'The Economic Costs of Non-Compliance with Medications in Australia', Australian Journal of Pharmacy, 69, 1988, p 129.
34. Australian Institute of Health, unpublished, 1992.
35. Commonwealth Department of Health, Housing and Community Services, Annual Report, Australian Government Publishing Service, Canberra 1991, p.53.
36. Soumerai S B, Degnan D R et al, 'Effects of Medicaid Drug Payment Limit on Admissions to Hospitals and Nursing Homes', New England Journal of Medicine, 325 (15), 1991, p. 1072.

References (cont.)

37. McGavock H; 'Using Imperfect Pharmaceutical Pricing Databases to Promote More Cost-effective and Scientific Prescribing in General Practice', paper presented to National Academic Detailing Workshop, St Vincent's Hospital, Sydney, 1992.
38. 'Too Much of a Good Thing: A study of Older Consumers and Their Medications', Australian Consumers' Association and the Australian Pensioners' and Superannuants' Federation, 1987.
39. 'Rational Prescribing: the Challenge for Medical Educators', conference proceedings published in Australian Prescriber, Vol 14, Supplement 1, 1991.
40. K Harvey, 'Antibiotic Use in Australia', Australian Prescriber, Vol 11, 4, pp. 74-77.
41. Report of the 41st World Health Assembly Meeting, 1988.
42. Report on the Self-Regulation of Promotion and Advertising of Therapeutic Goods, Trade Practices Commission, Canberra, July 1992.

LIST OF APPENDICES

- Appendix I:** 'Analysis and Critical Review of the Literature with respect to Appropriateness and Correctness of Medicinal Drug Use in Australia', prepared by Dr Susan D Whicker
- Appendix II:** List of Past Reports, Inquiries etc. relevant to the Quality Use of Medicines
- Appendix III:** 'Principles of Health Education' paper prepared by Mary Hodge (Chair) and Dr Andrew Gilbert, the Pharmaceutical Health And the Rational use of Medicines (PHARM) Working Party
- Appendix IV:** 'Why an Educational Strategy is Essential to the Government's Rational Drug Use Policy', Dr Andrea Mant

Appendix I: 'Analysis and Critical Review of the Literature
with respect to Appropriateness and Correctness
of Medicinal Drug Use in Australia', prepared by
Dr Susan D Whicker

SECTION 1

1.0 Comments on the document:

A communication strategy for the promotion of rational use of PBS drugs

Assessing information sources used for this document proved to be difficult due to:

- * lack of referencing details given within the document.
- * the use of specific sections of information which are passed between government reports and press releases without (a) being referenced to any sources (e.g. ".....20,000 admissions to hospitals per year are a result of illness attributable to pharmaceuticals..." or (b) being referenced in a "carte blanche" fashion through the title of the government document from which the information was obtained
- * inability to access certain government documents.

The only major query with the document involved the statement "...social costs of non-compliance with pharmaceutical drugs in Australia may be as high as \$700 million per year of \$1000 million spent on pharmaceuticals, which is approximately 4% of all expenditure..." (Section 7; page 12).

This statement is taken almost directly from the abstract of the paper "The economic costs of non compliance with medications in Australia" by Plant & Gross (1988). Interestingly, explanations and/or calculations for the figure of \$700 million are not located within the text of the paper. The identical statement and figures have also been presented in the Pharmaceutical Policy (Draft, June, 1990; page 5).

Provision of estimated costs for any health care service is difficult, thus calculation of estimated social costs due to patient non compliance is going to pose even greater difficulty. For calculations on the economic costs of non compliance, the figures for hospital admissions due to patient non-compliance were taken from the thesis "Patient compliance with medication on admission to and discharge from hospital" by Ausburn (1979).

In this study, one of the selection criteria for classification of the non-compliant patient was the omission of >1 dose per week. Overall, 37.1% of the 205 patients studied were classified as non compliant. Adjustment of the sample size to include only those patients on regular drug treatment increased the figure for non-compliance in patients to 45.3%. Thus, it is not surprising that the figure for non-compliant patients is relatively high. Hospital admissions in this study of non-compliant patients totalled 25.9%:

- * 20.5% were "probably non-compliant" patients with exacerbation of disease for which the medication was prescribed
- * 5.4% were "possibly due to non-compliance" if admission was an indirect consequence of non-compliance.

Few studies on patient non-compliance with such scope had been carried out in the 1970s prior to that of Ausburn. Since then, however, more stringent selection criteria for causation apply, thereby influencing the overall incidence of admission of so called non-compliant patients.

Finally, the overall impression gained from descriptive statistics of the work of Ausburn (1979), is that the non-compliant medical admission patient of a large inner city teaching hospital (Royal Prince Alfred Hospital, Sydney) tended to be a heavy drinker of lower socioeconomic status who was less likely to have a malignant or haematological diagnosis and was prescribed a greater number of daily doses of medication.

I can only suggest that, in all likelihood, the patients studied by Ausburn (1979) do not provide valid baseline data on the non-compliant patient from which extensive calculations on the economics of non-compliance for Australia are based (Plant & Gross 1988).

1.1 References

Ausburn L. 'Patient compliance with medication on admission to and discharge from hospital'. MSc(Pharmacy) thesis, University of Sydney, 1979.

Pharmaceuticals Policy (Draft). Alcohol and Drug Foundation, 1990, p5.

Plant A & Gross P. 'The economic costs of non compliance with medications in Australia'. Aust J of Pharm, 69, 1988, p12.9

SECTION 2

2.1 The need for appropriate prescribing and drug use

2.1.1 Introduction

The extent of use of the Australian health care system was highlighted recently with the release of the Australian National Health Survey 1989-1990 figures (Australian Bureau of Statistics ABS, 1991). In the two weeks before the survey was conducted, 20% of the population consulted a doctor. Medication was used by 76% of women and 65% of the men surveyed. The majority of persons also reported the use of some form of non-prescribed medicine (Mant, Whicker & Kwok, 1992). Pain relievers, vitamin and mineral supplements, skin ointments and medications for cough or cold were the major groups of non-prescribed medications used (Figure 2.1.1) and age-specific rates of use of medications (prescribed and non-prescribed) can be seen in Figure 2.1.2.

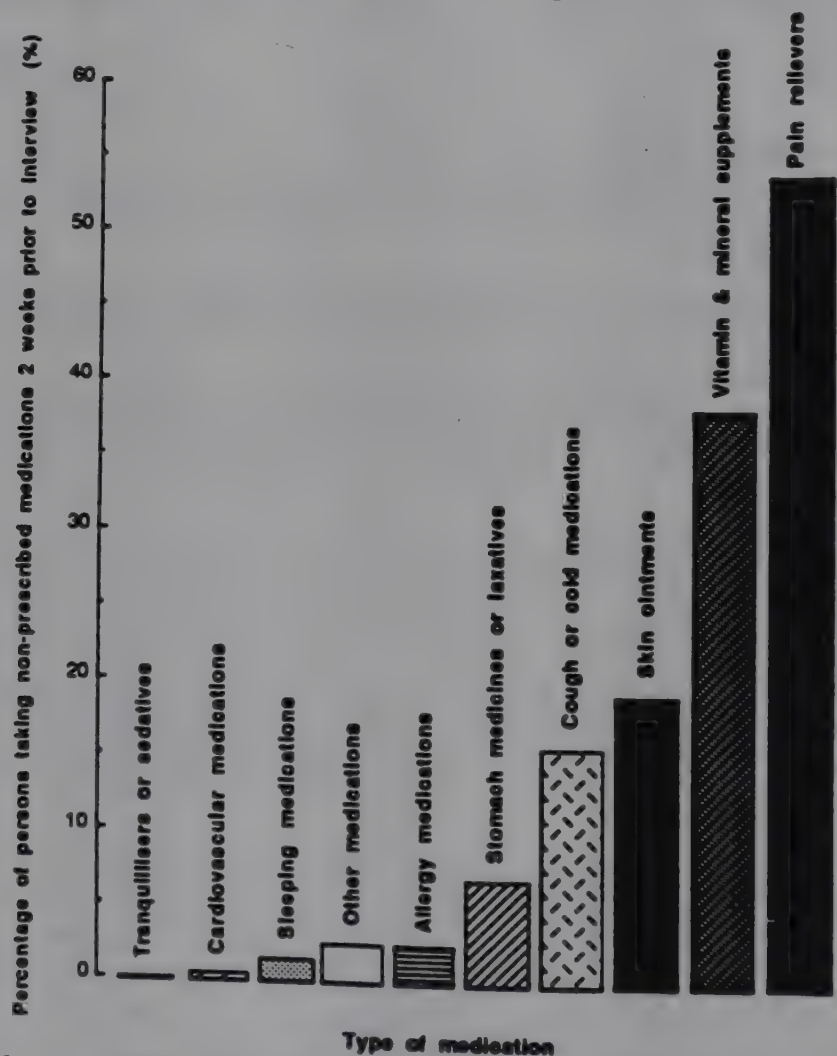
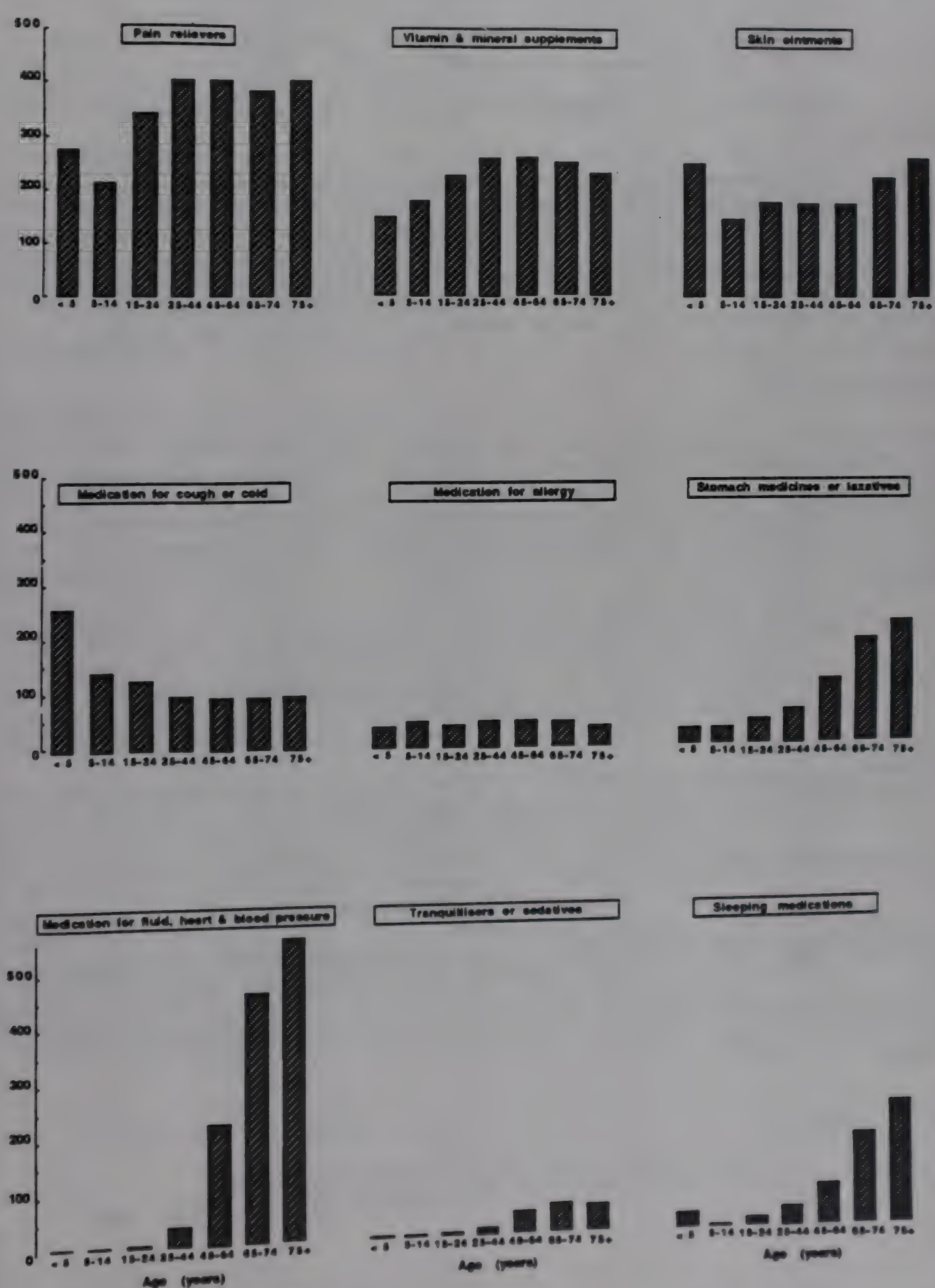


Figure 2.1.1 Use of non-prescribed medications in Australia: National Health Survey, 1989. (Source data unpublished. Tables provided by ABS).

The Australian Government, through the Pharmaceutical Benefits Scheme (PBS) and Repatriation Pharmaceutical Benefits Scheme (RPBS), subsidizes approximately 70% of drugs supplied through retail pharmacies. Cost of the PBS to the Government was \$1.2 billion for 1989-1990. Inappropriate

Figure 2.1.2 Age specific rates of use of medications in Australia: National Health Survey 1989-90 (Australian Bureau of Statistics 1991).



prescribing and use of medication is postulated to constitute the majority of the expenditure on the PBS (Fitzwarryne, unpublished; Coper, 1992). Thus, as a means of curbing further increases in PBS costs, a public education program for the PBS was devised. The campaign aims to raise public awareness of the cost of wasted medicines to the community, and the benefits of appropriate use of prescribed and non-prescribed ("over-the-counter" or OTC) medicines to health and quality of life (A communication strategy for the promotion of the national use of PBS drugs, 1991).

2.1.2 Indications of inappropriate prescribing and use of medications

Public campaigns which collect returned unused medicines indicate inappropriate prescribing and use of medicines, as well as the therapeutic categories involved.

Incidence figures for accidental or therapeutic poisonings are reliant upon the correct medication, and therefore the cause of the poisoning, being accurately written up in the hospital patient notes.

MediDump 1987

In regard to medicines returned for the 1987 MediDump campaign conducted in Western Australia (Longmore, McDonald, Sutherland et al., 1990): 68.8% were obtained by prescription, 25.4% were 'over-the-counter' (OTC) medicines and 18.8% were totally unused. Over half of all drugs returned were from the following categories of therapeutic agents:

CNS (central nervous system)	analgesics
	tranquillisers
	antidepressants
	antibiotics
	sedatives
musculoskeletal	
skin	ointments and creams
alimentary	antacids
	water
	electrolytes
cardiovascular	heart
	blood vessels.

Prescription-originated returns consisted primarily of drugs from the CNS, skin, cardiovascular and antibiotic categories.

In regard to prescription medicines returned, other important information, apart from the incidence and therapeutic categories, included:

- * 9.5% were not specifically labelled for the patient
- * only 21.6% carried a dispensing date
- * only 8.6% carried cautionary labels, with the

majority of those suggesting storage conditions or warning of possible medication-induced side effects, especially when combined with alcohol
* that medicines returned were not influenced by socioeconomic characteristics.

However well designed such studies are, the validity of the values obtained is still questioned. Results relying upon the return of unused medications are unable to account for medications which may remain stored at home or in the desk drawers at the office, although Harvey (1987) was unable to demonstrate evidence of hoarding medications.

In conclusion, this study indicated the extent of wastage of prescription-obtained medications and therefore unnecessary cost to the community, due to payment for such medications through the Pharmaceutical Benefits Scheme. Also, many of these medicines lacked patient-specific instructions and cautionary labels, both of which may be contributing factors in improving compliance and patient safety.

Investigations into poisoning

Inappropriate use and awareness of medicines can also be demonstrated from investigations of the incidence of therapeutic poisoning as recorded by hospital admission and separation (discharge) information and mortality registers. The incidence of, and the agents responsible for, poisonings in Western Australia between 1984 and 1988 have been reported in a retrospective study of data from the Hospital Morbidity Data System, W.A., and mortality tapes from the Register General, W.A. (Waddell & Serafino, 1991). In 1988, poisoning was responsible for 1.5% of all hospital discharges and 1.0% of all recorded deaths in W.A. Accidental poisoning was defined as the taking of the incorrect drug by mistake, whilst therapeutic poisoning encompassed inappropriate prescribing, non-compliance and adverse drug effects with correct administration.

Over the 8 years from 1981 to 1988, therapeutic poisoning became the most common poisoning requiring hospitalisation, whilst in 1981 self-inflicted poisoning was the most common. The age-standardised rate of incidence almost doubled from 59.42 (1981) to 116.32/100,000 people years (1988) for therapeutic poisoning, whilst that for self-inflicted poisoning decreased. By 1988, medicinal agents affecting the cardiovascular system were the most frequent source of therapeutic poisoning (Tables 2.1.1 and 2.1.2) and the age group most likely to be hospitalised for therapeutic poisoning was 65+ years.

Table 2.1.1 The five most common therapeutic categories responsible for therapeutic poisoning in males, Western Australia 1984-1988

Ranking of Categories	Age Groups (years)		
	15-39	40-64	65+
1.	systemic drugs	cardiovascular	cardiovascular
2.	psychotropics	systemic drugs	diuretics+
3.	antibiotics	antibiotics	analgesics+
4.	others+	hormones+	hormones+
5.	analgesics+	analgesics+	systemic drugs

Abbreviations:

systemic agents: antiallergic and antiemetic drugs; antineoplastic and immunosuppressive drugs; alkalizing agents; enzymes and vitamins cardiovascular agents: parasympathetic and sympathetic agents; cardiac glycosides; ganglion blockers; vasodilators; other antihypertensive agents, sclerosing agents.

hormones+: adrenal cortical steroids; androgens and anabolic agents; ovarian hormones and substitutes; insulins and antidiabetic agents; pituitary hormones; thyroid and antithyroid agents.

psychotropics: antidepressants; tranquillisers - major and minor; hallucinogens; psychostimulants.

diuretics+ (water, mineral and uric acid metabolism agents): purine derivative diuretics; carbonic acid anhydrase inhibitors; saluretics; minerals; uric acid metabolism drugs.

analgesics+ (analgesics, antipyretics and antirheumatics): opiates; salicylates; aromatic analgesics; pyrazole derivatives; antirheumatics; other analgesics.

antiinfectives: sulfonamides; arsenical agents, antiviral, antimycobacterial drugs); antihelminthics.

Table 2.1.2 The five most common therapeutic categories responsible for therapeutic poisoning in females, Western Australia 1984-1988

Ranking of categories	Age Groups (years)		
	15-39	40-64	65+
1.	hormones+	hormones+	cardiovascular
2.	antibiotics	systemic drugs	diuretics
3.	psychotropics	cardiovascular	analgesics
4.	others+	others+	hormones+
5.	anticonvulsants	analgesics	psychotropics

Abbreviations (Table 2.1.1)

Overall, the incidence of mortality due to therapeutic poisoning was extremely low, with only 5 deaths being attributed to therapeutic poisoning from 1984 to 1988.

In children, medications most frequently responsible for accidental poisonings were analgesics+, tranquillisers and other drugs. Mortality (1984-1988) due to accidental poisoning in the 0-14 years age group was low with only a total of four deaths, all of these being girls. Causes of death were recorded as petroleum products and solvents and "other drugs" (Table 2.1.2 for definition of therapeutic categories).

Unfortunately, the available information on morbidity and mortality does not take into account the ethnic background of the individuals, although provision was made for aboriginality. Care must be exhibited with the interpretation of these rates due to low numbers within each of the age groups. Rates of poisonings for Aborigines were almost double those for non-Aborigines. Accidental poisoning of 0-14 year old Aboriginal males and self-inflicted poisonings (with solid, liquid and vaporous substances) for adult (15+ years of age) Aboriginal females presented the highest rates of poisoning in this population.

In summary, the pattern of poisoning in W.A. has changed since 1973, with therapeutic poisoning replacing self-inflicted poisoning (1981) as the most frequent cause of poisoning for hospital admissions, and particularly in the 65+ years age group. However, for children and young adults, accidental poisoning and self-inflicted poisoning respectively are the most common cause of poisoning resulting in hospital admission. Thus, possible poisoning prevention strategies will need to be broadly based to encompass each of these different types of poisoning and age groups.

Further support for awareness of adverse drug reactions (ADRs) with correct administration of medicines is provided by results from a recent prospective study of hospital admissions due to drug reactions (Larmour, Dolphin, Baxter et al., 1991). In this study, all suspected cases of drug-related admissions to Prince Henry Hospital, Monash, Victoria were comprehensively reviewed by three of the authors. Classification of the drug reactions was according to the World Health Organisation criteria.

Of the 5623 hospital admissions, 2.4% were considered to be drug-related - 1.6% due to ADRs and 0.7% due to drug overdose or accidental poisonings. The drugs most frequently implicated in the ADRs of these patients coincided with those implicated in therapeutic poisonings in the retrospective study from Western Australia (Waddell & Serafino, 1991) i.e. cardiovascular and analgesic (including non-steroidal anti-inflammatories) agents. These ADRs occurred more frequently in elderly patients, again coinciding with information provided by the W.A. study (Waddell & Serafino, 1991). Of the ADRs recorded in the Victorian study, one-third were due to drug interactions, of which about one quarter of these patients had a documented history of at least one ADR. The increased likelihood of further ADRs in such patients indicates a need for careful prescribing of any medications in these patients.

Results from this prospective study again suggest the importance of appropriate prescribing and use of medicines, especially in the elderly population. Such a need is not only for the general well-being of the patient, but also for a reduction in the health care expenditure directly due to inappropriate prescribing and/or use of medications.

Extension of the work on drug-related hospital admissions is the incidence of drug-related readmission and therefore further costs incurred to the health care system from increased duration of hospitalisation.

Such information is provided by a six-week survey of patient readmissions to the Fremantle Hospital, January-February 1991 (Blackbourn, 1991a & 1991b). Overall, 12% of readmissions (180 of 1564) to Fremantle Hospital were unplanned and occurred within 60 days of discharge. Drug-related readmissions accounted for 16% (29 of 180) of these. Incidence of readmission for non-compliance and ADRs were almost equal. Medications responsible for the majority of these readmissions were cardiovascular and analgesic (including non-steroidal anti-inflammatories) agents, again coinciding with medications implicated in the previously mentioned studies for therapeutic poisoning in W.A. (Waddell & Serafino, 1991) and drug-related admissions to Prince Henry Hospital, Victoria (Larmour et al., 1991). Again, the majority of these patients readmitted for drug-related effects were elderly (mean age of patients with drug-related readmissions was 64 years).

Increased costs to the health care system incurred by the daily cost per occupied bed totalled \$140,000 for these 29 admissions, of which a significant proportion could have been avoided with more appropriate prescribing and use of medications, including the counselling of the patient and/or support persons of appropriate use of the medications prescribed.

Childhood poisonings

Investigation of the changing pattern of childhood poisoning between 1983 and 1988 for children admitted to the Childrens Hospital, Sydney, has recently been completed (Campbell and Oates, 1992).

In this study, the term "poisoning" is defined only as the ingestion of poisons, and not adverse reactions to therapeutic doses of medication. Admission of children for poisoning (455 children, records available for 407) represented 0.5% of all admissions. Of these, 66% had ingested medications, with benzodiazepines, iron preparations, paracetamol and anticonvulsants being the major medications involved. The ten most common substances involved, and the incidences of childhood poisonings for 1983-88 are demonstrated in Table 2.1.3.

able 2.1.3: The ten most common substances involved in childhood poisoning 1983-1988.

	Number of children	Incidence %
Benzodiazepines	41	10
Iron preparations	30	7
Paracetamol	27	7
Anticonvulsants	21*	5
Caustic soda	16	4
Dishwashing powder	15	4
Quinine	14	3
Antihistamines	13	3
Digitalis	13	3
Eucalyptus oil	12	3

Fifteen of the 21 children ingested carbamazepine

Comparison of the incidence and type of poisoning in the present study with results from an earlier study conducted within the same hospital (Beveridge, 1956) demonstrated that poisoning with the therapeutic agents benzodiazepines and iron preparations had replaced poisoning with household agents such as kerosene and pesticides.

Surprisingly, a higher incidence of poisoning in those children of non-English speaking backgrounds was not seen. Speculation regarding difficulties in communicating with families about dosage and the prevention of poisoning would have suggested otherwise.

Researchers of the present study also assessed the knowledge of general practitioners (GPs) and pharmacists of the possible toxicity of medications most commonly responsible for childhood poisonings. Results suggested that the majority of GPs and pharmacists who returned the questionnaire were unaware of the high toxicity of anticonvulsants and paracetamol in a paediatric situation. However, precautionary advice when dispensing medications was provided by the majority of participating GPs and pharmacists.

In conclusion, the overall incidence of morbidity and mortality of poisoning in children is low, however such poisonings are still largely preventable. Increased awareness of parents, GPs and pharmacists to possible toxicity and safe storage of commonly prescribed medications in children may be necessary in reducing the incidence of childhood poisonings.

Poisoning in the elderly

Poisoning in the elderly is a major problem, as noted earlier in the incidence of therapeutic poisoning in the 65+ years age group (Waddell and Serafino, 1991). This is not surprising, as in Australia older people average more than 27 prescriptions per year (Marr, 1992).

Klein-Schwartz and Oderda (1991) have presented a comprehensive review of all aspects of poisoning in the elderly. Information on the diagnosis and management of therapeutic poisoning is particularly detailed and would be useful for health professionals in an accident and emergency setting, however such issues are peripheral to the area of appropriate drug use and therefore will not be covered in the present document.

Of poisonings reported to the American Association of Poison Control Centre National Data Collection System in 1989, 2% involved persons of at least 60 years of age. The incidence of accidental poisoning in older people (84.3%) was 1.3-fold greater than that for younger people (64.3%), and the incidence for older women was almost 2-fold greater than that for older men (1.7:1.0; Litovitz, Schmitz & Bailey, 1990). Poisonings recorded by a regional poison centre also demonstrated that for older persons 83.1% of poisonings were unintentional (Klein-Schwartz, Odera & Booze, 1983). Mortality rates from the Maryland Poison Centre in 1989 demonstrated that although only 1.5% of reports were for persons of at least 60 years of age, this group accounted for 22.6% of deaths (Maryland Poison Centre 1989 Statistical Report, 1990).

The majority of poisonings occurred in the home (63.7%) and 14.3% in nursing homes. Reasons for the unintentional poisonings were:

- * dementia and confusion
- * improper use of the product ie. exposure whilst the product is being used for intended purpose eg. inhalation of ammonia fumes
- * improper storage of the agent ie. transfer of product out of original container
- * mistaken identity.

Age-related changes in physiological functioning/distribution, metabolism, renal and hepatic excretion predisposes older persons to unintentional therapeutic poisoning, with the risk increasing with the presence of concurrent medication pre-existing disease processes.

Interestingly, the suggested strategies for prevention of therapeutic poisoning in the elderly were directed at prevention of exposure and minimisation of the injury that occurs from the exposure. Limitation of access to medication for the elderly with difficulties caring for themselves include the use of locked storage cabinets and modification of medication administration. Misuse of medication due to mistaken identity may be reduced with standardisation of container design for specific categories of products and the use of larger type on the labels. Strategies likely to reduce injury in the event of therapeutic poisoning are those which either reduce the concentration of the agent or reduce the amount available, either at dispensing or at administration, with devices that deliver one tablet at a time.

2.1.3 Summary

The papers presented in this section display different aspects of inappropriate and/or incorrect use of medications. What is particularly daunting is the high involvement of prescribed medication in the role of poisonings across all age groups of the population.

The overall number of medicines returned and the high incidence of specific therapeutic categories being returned in the 1987 MediDump campaign provides overwhelming evidence as to why benzodiazepines, analgesics and cardiovascular drugs are those medications commonly responsible for childhood poisonings and as to why the majority of poisonings in children and older populations occur in the home.

One can only speculate as to the reasons for medications to be accidentally ingested left lying about the home, stored incorrectly or hoarded. To avoid continuing recurrence of these situations, issues such as why the medication was available and why the patient had not complied to the proposed medication regime need to be addressed. Why? The emotional cost of morbidity and mortality to individuals and families involved in any type of poisoning is large. However, the financial costs involved in the

dispensing of medications, of which some, if not all, may be wasted due to noncompliance, and the medical costs incurred from hospitalisation for the treatment of poisonings with therapeutic agents is enormous.

Strategies aimed at reducing each of these losses need to be implemented. Campaigns raising awareness of health professionals and consumers regarding appropriate medication management plans for the treatment of specific complaints may contribute to the reduction of morbidity and mortality with improved patient compliance, which in turn may reduce health care costs to the community. Areas of medication utilization likely to benefit from such campaigns include: asthma medication, benzodiazepines, cholesterol lowering medications, hormone replacement therapy, cardiovascular medications, nonsteroidal antiinflammatory medication and antibiotics.

2.2.4 References

Australian Bureau of Statistics, 1991. 'Summary of the Australian National Health Survey 1989 - 1990'.

Beveridge J. 'Accidental poisoning in childhood'. Med J Aust, 1, 1956, p216.

Blackbourn J. 'Readmission to Fremantle Hospital. Part I - Who comes back - when and why?' Fremantle Hospital Drug Bulletin, 15(3), 1991a, p9.

Blackbourn J. 'Readmission to Fremantle Hospital. Part II - Drug-related readmissions'. Fremantle Hospital Drug Bulletin, 15(4), p13.

Campbell D & Oates RK. 'Childhood poisoning - a changing profile with scope for prevention'. Med J Aust, 156, 1992, p238.

Coper L. 'Raising medication awareness in the Australian community - the Med Aware Campaign'. Australian Pharmacist, 1992, p35.

Fitzwarryne P. 'Incidence and community cost of the inappropriate use of prescribed pharmaceuticals'. Per Towards national strategies and objectives for health advancement - Draft plan - Prepared by Commonwealth Department of Health, Canberra, May 1985.

Harvey R. 'Hoarding and wastage of prescription drugs'. Presented to the 1987 Public Health Association Conference, Sydney, August, 1987.

Klein-Schwartz W & Oderda GM. 'Poisoning in the elderly: epidemiological, clinical and management considerations'. Drugs & Aging, 1, 1991, p67.

Klein-Schwartz W, Oderda GM & Booze L. 'Poisoning in the elderly'. Journal of the American Geriatrics Soc, 31, 1973, p195.

Larmour I, Dolphin RG, Baxter H et al. 'A prospective study of hospital admissions due to drug reactions'. Australian J of Hospital Pharmacy, 21, 1991, p90.

Litovitz TL, Schmitz BF & Bailey KM. '1989-Annual Report of the American Association of Poison Control Centers National Data Collection System'. Am J of Emergency Med, 1990 (in press).

Longmore R, McDonald C, Sunderland B et al. 'Examination of a sample from a MediDump campaigning in Perth, Western Australia'. Australian Pharmacist, 9, 1990, p145.

Mant A, Whicker SD & Kwok YS. 'Over-the-counter self-medication: the issues'. Drugs & Aging, 1992.

Marr R. 'Draft - Report and recommendations for national policy action to improve the use of medications for and by the elderly'. Commonwealth Department of Health, Housing & Community Services.

Maryland Poison Centre. 'Statistical Report 1990'. Toxalert; 7, 1989, p1.

Waddell VP, Serafino S. 'Poisoning in Western Australia 1984-1988. An analysis of hospital morbidity and of mortality due to accidental and self-inflicted poisonings'. Health Department of Western Australia, Statistical Series/25, 1991.

2.2 Literature review on the appropriate prescribing and use of:

Anti Asthma Medications

2.2.1 Introduction

Asthma is a chronic disease characterised by airway inflammation. Symptoms of this disorder are related to variability in airflow to the patient. Thus, pharmacological management of this disease aims at reducing and maintaining corrected airflow limitation. Medications used can be classified under three major categories.

Therapeutic agents - medications aimed at reducing the underlying inflammation, thereby reducing and/or maintaining reduced airflow variability in asthmatic patients: -

- * inhaled corticosteroids - beclomethasone and budesonide
- * inhaled sodium cromoglycate
- * oral corticosteroids - prednisolone

Bronchodilators - provide relief from the symptoms

- * B₂ agonists - preferably inhaled although oral preparations are available - salbutamol, terbutaline
- * anticholinergics - inhaled ipratropium bromide
- * theophylline - oral preparations

Prophylactic agents - prevent reduction in airflow following exposure to known triggers e.g. exercise, allergens and emotional encounters.

- * inhaled B₂ agonists
- * inhaled sodium cromoglycate

The severity of the asthma determines which of these medications and/or combinations of medications may be used (Seale, 1991).

A change in emphasis of the role of specific medications in the management of asthma has taken place over the past five years. Greater understanding of the condition itself and the medications available have influenced this shift in management. Previously, treatment of asthma focussed primarily on the symptoms, thus B₂ agonists were generally the first line of treatment. More recently, preventative medication such as sodium cromoglycate and inhaled corticosteroids taken in combination with a B₂ agonist has become the suggested management regime, particularly for patients with moderate to severe asthma (Woolcock, Rubinfield, Seale et al., 1989; Henry, Landau, Mellis et al., 1990; Arpel, 1991; Woolcock & Jenkins, 1991).

2.2.2 Epidemiology

In 1988, the National Health and Medical Research Council (NH&MRC) reported that asthma mortality rates were higher in Australia than most comparable countries, and that up to 60% of asthma deaths appeared to be associated with avoidable factors. Asthma mortality rates are also rising in New Zealand and the United Kingdom (Jackson, Seale, Beaglehole et al., 1988). In 1990, over 800 people died of asthma in Australia whilst only 106 asthma deaths were recorded for 1975 (Seale, 1991). Possible factors contributing to increased asthma mortality rates include: increased prevalence of the disease as approximately one in ten adults and one in five children in Australia have asthma (Jenkins, Hurley, Jolley et al., 1988), increased severity of asthma (Mitchell, 1985; Dawson, 1986) and changes in the availability (prescription and/or "over-the-counter" OTC) of B₂-agonist drugs and use of asthma drugs (Henry, Sutherland Frances et al., 1989; Jenkins, Hurley, Bowes et al., 1990).

Although prescribing rates for B₂-agonists, sustained-release theophylline and inhaled corticosteroids did increase from 1975 to 1986, it is difficult to postulate possible relationships between asthma mortality and changes in prescribing habits (Jenkins, Hurley, Bowes et al., 1990). Further support to these findings is provided by a recent study in the United Kingdom (Rees, 1991).

2.2.3 Economic costs

The cost of asthma to the community through the need for health care, reduced work productivity and changes in the quality of life is high. Determination of an accurate estimate of economic cost to the community is difficult. However, the total cost of asthma in NSW in 1989 was estimated to be \$209 million (Mellis, Peat, Bauman et al., 1991). This cost averaged out to about \$40 per head of population or \$796 per asthmatic person in NSW. Provision of nationwide retail costs for asthma medications by the private sector estimates the total national cost to be \$227.46 million, with the total NSW cost being about 38% of the total market or \$86.43 million (see Table 2.2.1).

Table 2.2.1 Estimated nationwide cost of asthma drugs in 1988

Drug Category	Estimated Cost * (\$ million)
Beta-agonists (bronchodilators)	114.86
Inhaled corticosteroids	37.37
Xanthines	12.41
Degranulation inhibitors (Intal)	18.32
Anticholinergics	17.04
Other	26.47
Total national cost	227.46
Total NSW cost (38% total)	86.43

* Retail costs plus dispensing fees

Source: Mellis, Peat, Bauman et al., 1991.

Both severity and frequency of asthma attacks can be reduced by appropriate and effective prophylactic therapy (Du Toit, Salome & Woolcock, 1987; Woolcock, Yan & Salome, 1988). Unfortunately, however, far too frequently investigations suggest that asthma is poorly controlled, possibly due to inappropriate use of current knowledge and medications available (Barnett & Oberklaid, 1991; Seale, 1991; Henry, Sutherland, Francis et al., 1992). If the severity and frequency of asthma attacks can be reduced with appropriate long-term medical management, it would be assumed therefore that overall economic costs to the community would be reduced.

Due to the lack of primary prevention methods for asthma, if strategies for appropriate management of the condition were to be implemented, then increases in morbidity, mortality and economic cost to the community may be curtailed. To meet such a need, the National Asthma Campaign was implemented within Australia in 1990.

2.2.4 Asthma Management - National Asthma Campaign

The National Asthma Campaign includes strategies to increase awareness about asthma in the general population and among health professionals. The major goals of the campaign are that within three years (1990-1993):

- * most people with asthma will be correctly diagnosed
- * most people with asthma will be using an asthma management plan
- * there will be a decline in preventable deaths from asthma (Woolcock, Rubinfeld, Seale et al., 1989; Rubinfeld & Ruffin, 1991).

Aside from increasing medical practitioner awareness of current appropriate management and patient education needs,

pharmacists also have a major role in the implementation of such a campaign.

The National Asthma Campaign has requested pharmacists to recognise and refer previously unsuspected asthmatics and poorly controlled asthmatics and to educate clients as to correct use of asthma medication, medication-associated appliances, peak flow meters and patient management plans. Further details of asthma management and the role of the pharmacist are provided in the following articles: Asthma Management Plan for Pharmacists (1991); Asthma Management and the Pharmacist (1991); The Pharmacists' Asthma Management Plan (1991).

2.2.5 Medical Management of Asthma

Individualisation of the six step asthma management plan for each patient presenting with asthma should provide appropriate management of the disease (Table 2.2.2; Woolcock & Jenkins, 1991).

Table 2.2.2 The six step asthma management plan

1. Assess severity of asthma
2. Achieve target lung function
3. Maintain target lung function by avoiding triggers/aggravators
4. Maintain target lung function with optimal medication
 - Asthma - inhaled corticosteroid, sodium cromoglycate
 - Symptoms - bronchodilator (+/- theophylline)
 - Triggers - bronchodilator, sodium cromoglycate
5. Establish an action plan
6. Educate and review regularly

The aim of management is to assess the severity when the patient is not having an attack and then to reduce the severity by maintaining the patient's target lung function.

Source: The Asthma Management Plan, and the National Asthma Campaign.

Step 1: Assess severity of asthma

This allows confirmation of the diagnosis and determination of severity of the disease. Information required for assessment includes: severity and frequency of current symptoms, current medication and useage and peak expiratory flow (PEF) measurement. Each of these factors can be scored and a total score determined which provides a measure of the severity of asthma (Table 2.2.3).

Table 2.2.3 Assessment for calculation of the asthma severity score

Severity	Score	For asthma (daily)	For symptoms
Mild when	1 to 5	Sodium cromglycate, 15 to 20 mg	Bronchodilator aerosol needed
Moderate	6 to 8	Inhaled corticosteroid, 0.5 to 1 mg +/- sodium cromoglycate, 15 to 20 mg	Bronchodilator aerosol for symptoms or when PEF <90% target Sodium cromoglycate for triggers
Severe	9 to 12	Inhaled corticosteroid, 1 to 2 mg +/- sodium cromoglycate, 15 to 20 mg	Bronchodilator aerosol for symptoms or when PEF <90% target Sodium cromoglycate for triggers Prednisone for exacer- bations

Source: Woolcock, Jenkins 1991.

Step 2: achieve target lung function.

Optimal lung function is achieved with PEF value of at least 90% or with PEF variability <25%.

Step 3: maintain target lung function by avoiding triggers/aggravators.

The most important triggers of asthma attacks are allergens e.g. dust mites, pollen, animal proteins. Snoring, airway obstruction or gastric reflux may present as aggravators of asthma.

Step 4 : maintain target lung function with optimal medication.

Table 2.2.4 provides guidelines to drug therapy for the treatment of asthma.

Table 2.2.4 Guidelines for the treatment of asthma

Symptoms	Score	Bronchodilator use	Score	PEF variability	Score
Waking at night	4	>4 times/day	4	>25%	4
Daily symptoms; night OK	3	1 to 4 times/day	3	15 to 25%	3
Symptoms <daily, >once-weekly	2	<daily	2	10 to 15%	2
None for three months	1	<once/week	1	6 to 10%	1

The patient scores 0 to 4 for symptoms, 0 to 4 for bronchodilator use and 0 to 4 for variability of peak expiratory flow (PEF). The scores are added to give a total out of 12. 1 to 5=Mild, 6 to 8=Moderate, 9 to 12=Severe.

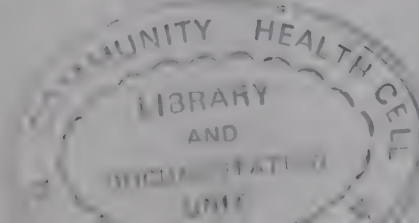
* Asthma severity should not be assessed during an exacerbation.

Source: Woolcock & Jenkins, 1991

B₂-agonist aerosols were once first-line therapy for asthma. Now, however, the management is with prophylactic agents. Recent investigations have provided further evidence negating a primary role of B₂-agonists. The studies suggest that potent bronchodilators such as fenoterol and terbutaline, whilst reducing the symptoms of asthma, may mask the presence of increased disease severity (Crane, Flatt, Jackson et al., 1989) or, that long-term use of aerosol B₂-agonist medications actually increases bronchial reactivity following cessation of treatment (Kerrebiijn, Van Essen-Zanduliet & Niejens, 1987; Vathenen, Knox, Higgins et al., 1988).

Theophylline (not included in the guidelines) does provide symptomatic relief to bronchoconstriction and is commonly prescribed in combination with other asthma medications. With the introduction of more recent asthma medications, the role of theophylline in asthma management should be reduced. In patients with severe disease requiring low doses of oral prednisone, however, theophylline does have steroid-sparing effects (Woolcock and Jenkins, 1991). Due to a narrow therapeutic range (10-20mg/Ll), care must be taken to avoid theophylline toxicity. Age and disease states must be taken into account when calculating dosage. Use of sustained-release preparations are recommended for ease of attaining and maintaining therapeutic levels of theophylline (Skinner, 1991).

One of the major problems with adequate control of airway flow limitation in asthma has been apprehension on the part



of the physician and/or patient regarding the use of corticosteroids. The benefits of aerosol corticosteroids are that, although improvement in PEF variation may take several weeks, only low doses of corticosteroids are necessary, thereby avoiding the well-documented side effects of corticosteroids. Also, the daily dose of inhaled steroid can be taken in two divided doses, thereby increasing the likelihood of patient compliance. A likely influence on patient non-compliance with this preparation is the incidence of dysphonia or oral thrush, although use of a spacer device and gargling after administration have been shown to reduce these problems.

Woolcock and Jenkins (1991) suggest that for oral steroid therapy:

- * do not be afraid of short courses of oral steroids
- * do not be afraid to use high doses (up to 1mg/kg/day)
- * do not be afraid to stop them rapidly once best lung function is achieved (if administered for less than 10 days)
- * do be afraid of long-term oral steroid therapy above 5mg/day.

No known non-pharmacological therapies have been demonstrated, in controlled studies, to provide and maintain target lung function. However, such treatments e.g. acupuncture and meditation, may enhance the well being of the patient and therefore contribute to maintenance of the disease. For those patients with an emotional component to their asthma, meditation and relaxation therapies may be useful. Active sport should be encouraged, particularly swimming.

Step 5: establish an action plan.

Individualised self management plans for patients include:

- * target and predicted PEF values
- * maintenance drug treatment
- * drug treatment for management of further reductions in PEF (PEF values to be included)
- * drug treatment and management if improvement is not shown in PEF following change in medication

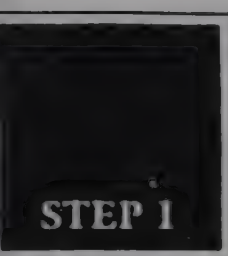
It is suggested that self management plans are accompanied by written instructions for the patient.

Step 6: educate and review regularly.

Implementation of appropriate medical management of asthma requires much input and awareness of the disease by the patient, with regular measurement of PEF, compliance to medication regime and avoidance of known trigger factors. Thus, the National Asthma Campaign also provided a six step

Asthma Management Plan for patients thereby providing educational material for self management (See Figure 2.1).

YOUR 6 STEP ASTHMA MANAGEMENT PLAN



Know how severe your asthma is.

If you recognise any of the following symptoms then you probably have moderate to severe asthma.

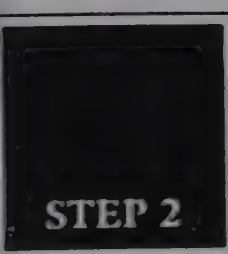
- If you need asthma medication most weeks of the year.

• If you wake at night with asthma.

• If you have needed urgent medical attention for asthma in the past year or so.

• If your peak flow measurement is consistently below expected, despite optimal treatment.

Assess the severity of your asthma and have it checked by your doctor.



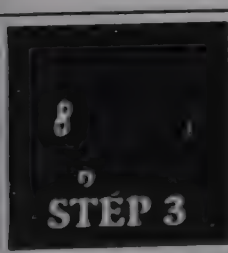
Achieve your best lung function.

When you are at your best you should ideally have:

- No symptoms.
- Best possible peak flow measurements and
- Your chest should sound normal when your

doctor examines you. It may take a few weeks of medication to achieve your best. Monitoring peak flow measurements at home can help you to check your progress.

When you have reached your best you will probably feel much better.



Avoid trigger factors.

Find out what sets off your asthma and try to stay away from it. These triggers could be:

- House dust, pollens, animal fur, moulds.
- Tobacco smoke.
- Things around your workplace or school.

like wood dust, flour dust, chemical fumes, fuel fumes, animals and many other things.

• Food preservatives, colourings and monosodium glutamate (MSG)

Air pollution and respiratory infections, such as colds or bronchitis, commonly trigger asthma but are difficult to avoid.

Exercise is generally good for you. It can trigger asthma but this can usually be easily controlled by taking the correct medication.



Stay at your best.

If you need medications these should be as simple, safe and effective as possible.

This is why inhaled medications are most often used for asthma.

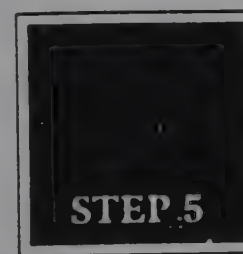
There are basically two types of inhaled medication that your doctor might advise you to use.

• The "preventer" (such as Becotide[®], Aldecin[®] or Intal[®]) is the main medication which keeps your asthma as steady as possible. But this will only work if you use it regularly.

• "The reliever" (such as Bricanyl[®], Respolin[®], Ventolin[®] or Atrovent[®]) is called a bronchodilator.

These relieve some symptoms, but usually for a short time.

Check which medications are best for you.



Know your action plan.

Together with your doctor you can work out a plan so that you can:

- Recognise when your asthma is getting worse.

• Know how to treat it quickly.

• Know how and where to get the right medical assistance.

Early attention to worsening asthma may prevent you from having a serious attack. Ask your doctor for an Action Plan card.



Check your asthma regularly.

Asthma can usually be kept under control. Follow your 6 point management plan and see your doctor for regular check-ups, not just in emergencies.

You can get advice and information from your doctor, your local pharmacy or the Asthma Foundation in your state.

Here are the Foundations' telephone numbers: New South Wales and ACT (02) 906 3233 • Victoria (03) 861 5666 • Queensland (07) 252 7677 • West Australia (09) 382 1666 • South Australia (08) 223 7235 • Northern Territory (089) 22 8817 • Tasmania (002) 23 7725

Figure 2.1 The National Asthma Campaign's Six Step Asthma Management Plan for Patients

Source: Rubinfield, Ruffin 1991

2.2.6 Conclusion

There is now considerable evidence to suggest that increasing mortality and morbidity of asthma may be largely preventable with appropriate management of the disease, thereby reducing economic costs to the community.

It is hoped that evaluation of the recently implemented National Asthma Campaign will demonstrate reduced incidence of asthma mortality and morbidity.

2.2.7 References / Additional reading

Abramson M & Bowes G. 'Asthma deaths : where now?' Med J Aust, 1991, 154, p12.

Alpers JH. 'The changing approach to the pharmacotherapy of asthma'. Australian Prescriber, 14, 1991, p71.

'Asthma Management Plan for Pharmacists'. Australian Pharmacist, 10, 1991, p18.

'Asthma management and the pharmacist'. Australian Pharmacist, 10, 1991, p128.

Barnett PJ & Oberklain F. 'Acute asthma in children: evaluation of management in a hospital emergency department'. Med J Aust, 154, 1991, p72.

Bittar G & Friedman HS. 'The arrhythmogenicity of theophylline. A multivariant analysis of clinical determinants. Chest, 99, 1991, p1415.

Crane J, Flatt A, Jackson R et al. 'Prescribed fenoterol and death from asthma in New Zealand, 1981-83: case control study'. Lancet, 1, 1989, p917.

Dawson KP. 'The severity of asthma in children admitted to hospital : a 20-year review'. NZ Med J, 100, 1987, p520.

Du Toit JI, Salome CM & Woolcock AJ. 'Inhaled corticosteroids reduce the severity of bronchial hyper-responsiveness in asthma but oral theophylline does not'. Am Rev Respir Dis, 136, 1987, p1174.

Henry DA, Gibson P, Cruickshank D et al. 'Non-prescription use of bronchodilator aerosols'. Med J Aust, 156, 1992, p68.

Henry DA, Sutherland D & Francis L. 'The Newcastle Retail Pharmacy Research Group, 1989. The use of non-prescription salbutamol inhalers by asthmatic patients in the Hunter Valley, NSW'. Med J Aust, 150, 1989, p445.

Henry R, Landau L, Mellis C et al. 'Childhood asthma : application of the international view of management in Australia and New Zealand'. J Paediatr Child Health, 26, 1990, p72.

Jackson R, Seale MR, Beaglehole R & Rea HH. 'International trends in asthma mortality 1970 to 1985'. Chest, 94, 1988, p914.

Jenkins MA, Hurley SF, Bowes G & McNeil JJ. 'Use of anti asthmatic drugs in Australia'. Med J Aust, 153, 1990, p323.

Jenkins MA, Hurley SF, Jolley DJ et al. 'Trends in Australian mortality of asthma, 1979-1985'. Med J Aust, 149, 1988, p620.

Kerrebiijn KF, Van Essen-Zanduliet EEM & Neijens JH. 'Effects of long-term treatment with inhaled corticosteroids and beta agonists on the bronchial responsiveness in children with asthma'. J Allergy Clin Immunol, 79, 1987, p653.

Mellis CM, Peat JK, Bauman AE et al. 'The cost of asthma in New South Wales'. Med J Aust, 155, 1991, p522.

Mitchell EA. 'International trend in hospital admission rates for children'. Arch Dis Child, 60, 1988, p376.

National Health and Medical Research Council Working Party on Asthma Associated Deaths: 'Asthma in Australia : strategies for reducing morbidity and mortality'. Canberra, NH&MRC, 1988.

Newcastle Retail Group. 'Post marketing surveillance of drugs : a role for retail pharmacists with microcomputers'. Aust J Pharm, 67, 1986, p294.

Paterson JW & Mant AW. 'Asthma therapy and mortality'. Med J Aust, 153, 1990, p312.

Rees J. 'B2 agonists and asthma. Still the mainstay of symptomatic treatment'. Br Med J, 302, 1991, p1166.

Rubinfeld A & Ruffin R. 'The National Asthma Campaign'. Current Therapeutics, 32, 1991, p11.

Seale JP. 'A pharmacological review of anti asthma medications'. Modern Medicine, (May Suppl), 1991, p36.

Seale JP. 'Asthma deaths : where are we now?' Aust NZ J Med, 21, 1991, p678

Skinner MH. 'Adverse reactions and interactions with theophylline'. Current Therapeutics, 32, 1991, p17.

'The Pharmacists' Asthma Management Plan 1991'. Australian Pharmacist, 10, 1991, p274.

Valhener AS, Know AJ, Higgs BG et al. 'Rebound increase in bronchial responsiveness after treatment with inhaled tebutaline'. Lancet, 1, 1988, p554.

Van Asperen PP, Mellis CM & Sly PD. 'The role of corticosteroids in the management of childhood asthma'. Med J Aust, 156, 1992, p48.

Van Schayck CP, Dompeling E, Van Herwaarden CCA et al. 'Bronchodilator treatment in moderate asthma or chronic bronchitis: continuous or a demand? A randomised controlled study'. Br Med J, 303, 1991, p1426.

Warner JD, Gotz M, Landau LI et al. 'Management of asthma: a consensus statement'. Artc Dis Child, 64, 1989, p1065.

Woolcock AJ & Jenkins CR. 'Management of asthma : a decreasing role for bronchodilators'. Modern Medicine, 34, 1991, p18.

Woolcock A, Rubinfeld AR, Seale P et al. 'Asthma Management Plan'. Med J Aust, 151, 1989, p650.

Woolcock AJ, Yan K & Salome CM. 'Effect of therapy on bronchial hyperresponsiveness in the long term management of asthma'. Clin Allergy, 18, 1988, p165.

Additional Reading

'Asthma'. Australian Family Physician, 20, 1991, p8.

Barnes PJ. 'A new approach to the treatment of asthma'. N Engl J Med, 321, 1989, p1517.

2.3 HORMONE REPLACEMENT THERAPY (HRT)

2.3.1 Introduction

Overall, the risk-benefit and cost-benefit ratios support the use of prophylactic long-term hormone (oestrogen & progestogen) replacement therapy (HRT) in the majority of women from an age at which oestrogen deficiency symptoms begin, or menstrual cycling ceases (MacLennan, 1991; Critchley, Farrell & Healey, 1992). However, the risk-benefit ratio will vary for each patient, as it is dependent upon an individual's characteristics and medical history. Moreover, it should be borne in mind that there is always some doubt about the safety of the long-term use of any medication.

To date, the major advantages of long term HRT to these women are:

- Improvement in quality of life
- Reduction in cardiovascular disease risk
- Prevention of osteoporosis

For further details see section 2.3.5.

The major disadvantages of long term HRT include the costs for the medications and regular medical review. Of the side effects that do occur with HRT including breast tenderness, nausea and uterine bleeding, adjustment of the therapeutic regimen to suit the individual should reduce the severity and/or occurrence of such side effects. For further details see section 2.3.4; MacLennan, 1991; Webster, 1991.

2.3.2 Economic Costs

A recently published cost-effectiveness analysis of HRT in an Australian context demonstrated that HRT in symptomatic women was cost-effective when taking into account the risk of myocardial infarction and prevention of osteoporotic fracture (Chung and Wren, 1992). However, as discussed previously (see Section 1.0), care must be taken with any further interpretation and/or extrapolation of results from cost-benefit analysis as the analytical model is dependent upon assumptions and estimates for several parameters, including the use of estimates from countries other than Australia.

An estimate of A\$25 million for the current pharmaceutical bill for oestrogen therapy in Australia was provided by Associate Professor MacLennan in his comment on the cost-effectiveness analysis by Chung and Wren (MacLennan, 1992a). This figure is about one eighth of the lower estimate for the annual health care and community costs for hip fractures in Australia (see Section 2.3.5; Eisman, 1992) thus providing support for the economic advantages of HRT to the community.

2.3.3 Hormone Replacement Preparations Available in Australia

Table 2.3.1

Oestrogen and Progestogen Preparations Available for Hormone Replacement Therapy in Australia.

Preparations	Dose (mg)
OESTROGENS	
Oral	
Conjugated equine oestrogen ('Premarin')	0.3-2.5
Ethinylloestradiol ('Estigyn')	0.01-0.03
Oestradiol valerate ('Progynova')	1.0-4.0
Oestriol ('Ovestin')	1.0-4.0
Piperazine aestrone sulphate ('Ogen')	0.625-5.0
Non-oral	
Oestradiol implant	20, 50, 100
Oestradiol skin patches ('Estraderm')	0.025, 0.05, 0.1
PROGESTOGENS	
Oral	
Levonorgestrel ('Microlut', 'Microval')	0.03-0.09
Medroxyprogesterone acetate ('Provera')	2.5-20
Norethisterone ('Primolut N')	1.25-5.0
('Micronor', 'Noriday')	0.35-1.05

2.3.4 Hormone Replacement Regimens

Prior to commencement of HR treatment, all women should be counselled on the advantages and disadvantages of specific treatment regimens. With awareness of possible side effects such as breast tenderness, bloating, fluid retention, uterine bleeding and vaginal discharge, the patient will be better prepared and more likely to be compliant with the treatment.

* For Women Without a Uterus

Continuous oestrogen alone is recommended, thereby avoiding the return of symptoms during the treatment free period. Oestrogen type, dose and form of administration will be influenced by the age of the patient, medical history, prescribing clinician's experience and patient preference.

Non-oral oestrogen preparations - oestradiol implants or oestradiol transdermal patches - are ideal for women without

a uterus, particularly for those who experience gastrointestinal disturbances with oestrogen or have poor medication compliance. Patient tolerance to oestrogen should be assessed prior to commencement of implant or transdermal therapy with either an initial trial of oral HRT or, alternatively, lower strength implants or transdermal patches could be trialled before scheduling a higher dose.

Progestogens are generally not indicated for women who have had a hysterectomy. However, women with residual endometriosis after hysterectomy may need to take oral progestogen to prevent endometrial cancer.

* For Women With an Intact Uterus

Oestrogen Alone

Due to increased risk of endometrial hyperplasia and carcinoma, oestrogen alone is not recommended. However, for patients who do continue on such a regimen, an endometrial biopsy should be carried out annually.

Combined Oestrogen and Progestogen

Addition of a progestogen for 12-14 days of each cycle abolishes the increased risk of endometrial hyperplasia or carcinoma in women with an intact uterus. Continuous oestrogen with a progestogen for the first 12 days of each cycle is the regimen of choice, due to the simplicity of the dosing schedule and predictability of the bleeding pattern. Continuous combined oestrogen-progestogen HRT taken on a daily basis throughout the cycle induces amenorrhoea in most women studied. Although episodes of bleeding during the first 4 months of treatment is common, no pathological changes to the endometrium have been documented. For further details see MacLennan, 1992b; Webster, 1992.

2.3.5 Major Advantages of Hormone Replacement Therapy

* Quality of Life

Up to 80% of menopausal women will experience hot flushes, night sweats, sleeplessness, anxiety, depression, tiredness, loss of libido, dry vagina, uncomfortable intercourse and urinary frequency. As these symptoms are oestrogen-dependent, response to HRT should be favourable. Minor side effects are normally experienced at commencement of HRT, however nearly all can be abolished with titration of therapy.

For further details see MacLennan, 1991; MacLennan, MacLennan, O'Neill et al., 1992.

* Reduction in Cardiovascular Disease

In Australia, 40% of deaths among women are attributed to cardiovascular accidents, with the majority of these deaths in postmenopausal women. Oestrogen deficiency in postmenopausal women results in an increase in cardiovascular disease, in addition to its effect on bone mass. Reviews of the majority of studies investigating the possible role of HRT in cardiovascular disease suggest that HRT reduces risks of coronary artery disease and stroke by 30-50%.

Overall, HRT in postmenopausal women has been demonstrated to improve the high density lipoprotein (HDL) cholesterol: low density lipoprotein (LDL) cholesterol ratio by decreasing total cholesterol and LDL cholesterol levels, thereby reducing the risks of cardiovascular disease.

Further cardioprotective effects of oestrogens may be provided by the slight reduction of blood pressure due to oestrogen-induced vasodilatation.

Oestrogen-induced thrombosis has not been demonstrated to be a complication in postmenopausal women and therefore it should not be necessary to cease HRT prior to elective surgery. However, caution is suggested in women on HRT who currently smoke.

For further details see MacLennan, 1991 & 1992; Newnham & Burger, 1992; Wren, 1992.

* Prevention of Osteoporosis

Osteoporosis is the reduction in bone density leading to an increased risk of fracture. It is estimated that 20-30% of Australian women will develop osteoporosis if they live beyond 70 years of age. The direct cost of age-related fractures in Australia is currently A\$175 million per annum. It is also estimated that of those Australian women reaching 70 years of age, 20-25% will have been hospitalised with a fracture of upper or lower limb or spine. Conservative estimates for health care and community costs involved for hip fractures alone in Australia (with a female:male ratio of 2:1) are between \$A200 and A\$500 million annually. Projected figures for hip fractures in the year 2011 are 18,000 per year, with these fractures occupying an estimated 570,000 surgical bed days.

Menopausal women are particularly at risk of osteoporosis, due to significant bone loss within 5 and up to 15 years of onset of menopause. Reduced oestrogen is postulated to increase break down of the bone. Other risk factors influencing osteoporosis in these women include: age greater than 55 years, family history of osteoporosis, low physical activity, smoking, low body weight, inadequate dietary calcium intake and/or impaired calcium absorption and excess corticosteroid hormone levels.

Oestrogen therapy prevents bone loss in postmenopausal women, thus reducing their risk of osteoporotic fracture. Maximum effects of oestrogen therapy can be demonstrated if started within the first 3 years of menopause, when bone loss is at a maximum. Further prevention of osteoporosis may be provided by a reduction in life-style risk factors, increased physical activity and a daily intake of 1000 to 1500 mg of elemental calcium.

However, it should be noted that a consultancy done for the Department of Health, Housing and Community Services has shown, by use of metanalysis, that 300 50-year-old women need to be treated for 10 years to prevent one hip fracture. Moreover, the same analysis showed that if oestrogen therapy is stopped after 3-5 years, the ratio of observed/expected fractures increases from 0.4 to 1.0 i.e. it reverts to the previous situation.

For further details see Sambrook, 1991; Seeman, Eisman, Gutteridge et al., 1991; Eisman, 1992

2.3.6 Hormone Replacement Therapy and Cancer

*** Endometrial Cancer**

A 2 to 20 fold increased risk of endometrial hyperplasia and endometrial carcinoma (1: 1,000) has been associated with long-term administration of oestrogen alone. However, addition of progestogen for 12-14 days of each cycle eliminates the increased risk of endometrial cancer. Cervical and ovarian cancer rates are unaffected by HRT use and there is also evidence that lower bowel and rectal cancers may be reduced by approximately 50% in women taking HRT.

*** Breast Cancer**

The influence of HRT on breast cancer remains controversial, as opinions are based on retrospective and cohort studies rather than randomised prospective placebo-controlled trials. No study has shown that hormones initiate breast cancer. The use of sex steroid hormones has no significant effect on the risk of breast cancer with hormone replacement therapy and contraception, as concluded in a recent review of case control and cohort studies.

Breast cancer affects at least 1 in 15 women by the age of 75 years. However, this rate is further increased to 1 in 8 for women with a family history of breast cancer. From those studies demonstrating adverse effects, the relative risk of breast cancer from long-term HRT is 1.3 cases/1,000/year rather than 1 case/1,000/year in Australian women not taking oestrogen.

As breast cancer has a relatively high incidence in women, it would not be unusual for the clinician to be managing a

menopausal woman with a history of breast cancer. There is concern that certain types of breast cancer can be promoted by HRT, due to the presence of oestrogen or progesterone receptors in the tumor.

However, Eden (1992 b) suggests that in the management of the menopausal woman with breast cancer, it is difficult to deny such women access to HRT. Rather, the quality of life must be balanced against the theoretical risk of tumor protection. Thus, symptomatic menopausal woman should be assessed on an individual basis.

Assessment of risk factors (cardiovascular, osteoporosis and tumor pathology) in conjunction with a judgement on the influence of menopausal symptoms on the quality of life should determine the possible use of alternatives to HRT, such as progestogens for flushes and topical oestriol for vaginitis. If menopausal symptoms remain severe, then only after consultation with the oncologist and written consent from the patient should oestrogen and continuous medium dose progestogen therapy be commenced.

For further details see MacLennan, 1990; Eden, 1992 a & b; Khoo & Chick, 1992.

2.3.7 Contra-indications to HRT

The only contra-indications to HRT are severe liver disease and post-menopausal thromboembolic diseases.

2.3.8 Conclusion

Menopausal women with severe oestrogen-dependent symptoms, and with a high risk of cardiovascular disease or osteoporosis, should benefit from HRT with improved quality of life and reduction of the likelihood of cardiovascular disease and osteoporosis. Overall management of the menopausal woman involves all aspects of life-style including exercise, diet, smoking, alcohol and psychosocial factors, in conjunction with provision of a suitable HRT regimen.

2.3.9 References/Additional Reading

- Cheung AP & Wren BG. 'A cost-effectiveness analysis on hormone replacement therapy in the menopause'. Med J Aust, 156, 1992, p312.
- Critchley HOD, Farrell EA & Healey DL. 'Safety of post-menopausal hormone replacement'. Aust NZ J Med, 22, 1992, p103.
- Eden JA. 'Oestrogen and the breast. 1. Myths about oestrogen and breast cancer'. Med J Aust, 157, 1992a, p175.
- Eden JA. 'Oestrogen and the breast. 2. The management of the menopausal woman with breast cancer'. Med J Aust, 157, 1992b, p247.
- Eisman JA. 'Osteoporosis. Prevention, prevention and prevention'. Current Therapeutics, 33, 1992, p25.
- Henry D. Hormone Replacement Therapy: A Meta-Analytical Approach. Consultancy done for the Department of Health, Housing & Community Services, 1992. Unpublished.
- Khoo SK & Chick P. 'Sex steroid hormones and breast cancer: is there a link with oral contraceptives and hormone replacement therapy?' Med J Aust, 156, 1992, p125.
- MacLennan AH. 'Hormone replacement therapy and the menopause. Consensus statement for the Australian Menopause Society'. Med J Aust, 155, 1991, p43.
- MacLennan AH. 'Comment - Hormone replacement therapy can be cost-effective'. Current Therapeutics, 33, 1992a, p87.
- MacLennan AH. 'Transdermal oestrogen replacement therapy'. Med J Aust, 156, 1992b, p679.
- MacLennan AH. 'Women, cardiovascular disease and hormone replacement therapy'. Med J Aust, 156, 1992c, p77.
- MacLennan AH, MacLennan A, O'Neil S et al. 'Oestrogen and cyclical progestogen in postmenopausal hormone replacement therapy'. Med J Aust, 157, 1992, p167.
- Newnham HH & Burger HG. 'Cardiovascular issues in the menopause'. Aust. Prescriber, 15, 1992, p 60.
- Sambrook PN. 'Osteoporosis: significance, diagnosis, prevention and management'. Modern Medicine, 34, 1991, p22.
- Seeman E, Eisman J, Gutteridge D et al. 'Osteoporosis: its causes, prevention and treatment - Statement on osteoporosis - The Royal Australasian College of Physicians'. Modern Medicine, 34, 1991, p37.

Webster M. 'Hormone replacement therapy. Which regimen?'
Current Therapeutics, 32, 1991, p41.

Wren BG. 'The effect of oestrogen on the female
cardiovascular system'. Med J Aust, 157, 1992, p204.

2.4 BENZODIAZEPINES

2.4.1 Introduction

Benzodiazepine use is controversial because of the dependence potential of therapeutic doses and the ambiguity in the indications for prescription of these medications.

Benzodiazepines are commonly prescribed as anxiolytics for treating anxiety, tension and as hypnotics for treatment of insomnia. Other indications include the treatment of epilepsy and status epilepticus (via intravenous injection), sedation as premedication or given intravenously for uncomfortable procedures such as endoscopy, and in the management of alcohol withdrawal. Intravenous administration can be of value in acute psychiatric emergencies where agitation is a prominent feature (Psychotropic drug guidelines, 1990).

2.4.2 Pharmaco-epidemiology

In Australia in 1989 and 1990, there were an estimated 750,000 users of benzodiazepines, of whom 330,000 used benzodiazepines on a daily basis and had done so for six months or longer (Australian Bureau of Statistics, 1991). Most of this use was for sleep disturbance. A total of 10.59 million prescriptions were dispensed through Australian pharmacies in 1990, enough for 3% of the population to take a daily dose (Mant, Whicker, Birkett et al., unpublished communication).

Benzodiazepine prescribing patterns are strongly influenced by government subsidisation, thus the majority of benzodiazepines prescribed within Australia were those listed on the Pharmaceutical Benefits Scheme i.e. diazepam, oxazepam, nitrazepam and temazepam (Table 2.4.1). Benzodiazepine utilisation, or defined daily dose/1000 persons/day (DDD/1000/day) for 1990 was 33.73 DDD/1000/day for Australia (Mant, Whicker, Birkett et al., unpublished communication).

Investigations into the prescribing of psychoactive medications in the Tasmanian community demonstrated that 13.2% of all prescriptions dispensed in Tasmania were for psychoactive medication (Jacobson, Friesen, Peterson et al., 1992). Importantly, the estimated prescribing rate for benzodiazepines was almost 1.5 times greater, at 47.8 DDD/1000/day, than the estimation for benzodiazepine utilisation for Australia in 1990. The pattern of prescribing for the individual benzodiazepines was similar to that shown for Australia.

Table 2.4.1

Percentage Distribution of Benzodiazepine Prescriptions in Australia, 1990. Data source: Australian Drug Utilisation Sub-Committee (DUSC) database, 1990.

Australia	
Benzodiazepine	%
diazepam	18.8
oxazepam	26.2
nitrazepam	15.4
temazepam	30.6
triazol	0.3
flunitrazepam	3.2
lorprazolam	-
lorazepam	1.3
chlordiazepoxide	0.6
others	3.5
Total	99.9

2.4.3 Pharmacology

Benzodiazepines facilitate the effects of the inhibitory neurotransmitter aminobutyric acid (GABA) via specific benzodiazepine receptors located within the GABA receptor complex. Multiple sub-types of benzodiazepine receptors within GABA receptor complexes in different areas of the central nervous system may account for the different clinical effects associated with different benzodiazepines. Although benzodiazepines have relatively similar chemical structures, these agents may differ greatly in lipophilicity, rate of absorption, metabolic pathways and rate of elimination, thereby influencing the potency and/or the duration of action of the agent.

The presence of an active metabolite can markedly lengthen the duration of action (Table 2.4.2). The selection of the benzodiazepine appropriate for specific clinical situations is based on their differing pharmacokinetic and pharmacodynamic properties.

Thus, benzodiazepines that are slowly absorbed and slowly eliminated are most appropriate for the anxious patient, due to a gradual and sustained anxiolytic effect. Rapidly absorbed and slowly eliminated benzodiazepines are usually more appropriate for patients with sleep disturbances, since rapid absorption induces sleep and the slower elimination rate may induce less tolerance to the sedative effect.

For further details see: Psychotropic drug guidelines, 1990; Teboul & Chouinard, 1990 & 1991; NH & MRC Guidelines for benzodiazepine use, 1992.

Table 2.4.2

The Pharmacokinetic Properties of Commonly Prescribed Anxiolytics and Hypnotics.

Drug	Elimination half-life [1] (hours)	Active metabolites	Elimination half-life of metabolites [2] (hours)
Anxiolytics			
Alprazolam	12+2	no	
Bromazepam	16[2]	yes	
Chlordiazepoxide	10+3.4	yes	75
Clobazam	2[2]	yes	40
Diazepam	43+13	yes	75
Lorazepam	14+5	no	
Oxazepam	6.8+1.3	no	
Hypnotics			
Flunitrazepam	15+5	yes	23,31
Flurazepam	2[2]	yes	80
Nitrazepam	26+3	no	
Temazepam	23+5	no	

Information sources:

- [1] Goodman Gilman A, Rall, Nies et al. Goodman & Gilman, The Pharmacological Basis of Therapeutics, 8th Edition.
 [2] Psychotropic drug guidelines. Victorian Medical Postgraduate Association, 1990.

2.4.4 Problems associated with benzodiazepine use

* Benzodiazepine dependence and withdrawal

(See Section 2.4.5)

* Oversedation and psychomotor impairment

Adverse effects include drowsiness, impaired alertness, agitation and ataxia. The elderly are particularly vulnerable to these effects, due to age-related changes in both pharmacokinetic and pharmacodynamic parameters. Higher rates of falls and hip fractures have been associated with the use of benzodiazepines with elimination half lives exceeding 24 hours. Therefore, caution should be exercised in the selection of a benzodiazepine for the elderly. For further details see Berry, 1990; Ames, 1991; Mant, 1992.

- * **Adverse effects on mood and behaviour**
- * **Rebound insomnia**
- * **Pregnancy and breastfeeding**

The teratogenic potential of benzodiazepines remains controversial. However, benzodiazepines have been associated with increased incidence of cleft palates and a characteristic dysmorphism, growth retardation and CNS dysfunction i.e. "floppy baby" syndrome.

Serious prolonged respiratory depression in new born infants can be induced by large doses of benzodiazepines administered to mothers during delivery. Continuous maternal use of benzodiazepines during pregnancy can lead to a neonatal benzodiazepine withdrawal or abstinence syndrome.

Benzodiazepines are excreted in the breast milk, and drowsiness has been reported in breastfed infants. Thus, mothers requiring benzodiazepine therapy should be using the lowest effective dose and their infants assessed for signs of benzodiazepine toxicity. For further details see Gaudreault, Guay, Thivierge et al., 1992; NH & MRC Guidelines on Benzodiazepine Use, 1992.

* **Overdose**

Benzodiazepines are relatively safe if taken alone in an overdose situation. Patients usually exhibit only mild CNS symptoms of somnolence, diplopia, dysarthria, ataxia and intellectual impairment. Flumazenil, a benzodiazepine antagonist, can be used in an emergency room situation for diagnostic purposes and reversal of benzodiazepine overdose.

Benzodiazepines, in combination with other sedative drugs, such as alcohol and antihistamines, can lead to severe CNS depression. For further details see Grandreault et al., 1992.

2.4.5 Dependence and withdrawal with benzodiazepine use

It is difficult to predict which patients will become dependent on benzodiazepines, although some groups of patients may be of greater risk i.e. those with a family and/or personal history of drug or alcohol dependence, and patients with maladaptive personality styles.

Indications of benzodiazepine dependence include: tolerance to usual dose of medication, rebound insomnia, inability to reduce medication use, self medication with more frequent and/or increased doses of benzodiazepines, and characteristic withdrawal symptoms.

Withdrawal can occur in persons who have been taking therapeutic or higher doses of benzodiazepines on a regular

basis for 2 or more weeks. Minor withdrawal symptoms are reported in up to 50% of patients discontinuing therapeutic doses of benzodiazepines. However, withdrawal between regular doses can occur, in particular with those benzodiazepines with a rapid onset of action and short duration of effect, such as those commonly prescribed for insomnia.

There is a significant risk of withdrawal if benzodiazepines are discontinued abruptly, particularly in the sick and elderly. Patients admitted to hospital should be given their usual benzodiazepine medication, in order to avoid withdrawal and not complicate their hospital stay. It is recommended that such patients commence their benzodiazepine withdrawal once discharged from hospital, under the supervision of a general practitioner.

Withdrawal from short acting benzodiazepines generally occurs earlier and is more severe than withdrawal from long acting benzodiazepines. Severity of benzodiazepine withdrawal is also dependent on the duration of action and the dose of the drug, the rapidity of withdrawal and the personality characteristics of the patient.

The benzodiazepine withdrawal is characterised by the following signs and symptoms: anxiety, insomnia, abnormal body sensations, increased sensory perception, a sense of derealisation and depersonalisation, muscle twitching and aching, tremor, parasthesia, tinnitus, blurred vision and restlessness.

It is easy to underestimate the severity of benzodiazepine withdrawal, as the patient may appear calm. Upon questioning of the patient, however, it may become apparent that the patient is confused and may have a fluctuating level of consciousness.

Major manifestations, such as seizures and delirium, are rare. Seizures may occur 1-12 days after discontinuing benzodiazepines. Delirium is a significant problem, as is confusion in elderly patients.

The majority of medically supervised benzodiazepine withdrawal programmes occur in an outpatient setting. Individualised withdrawal programmes need to be planned, with the consent of each patient. The minimum time to slowly reduce benzodiazepine use in this setting is about 4 weeks. Each dose reduction should be titrated against the patient's withdrawal symptoms. For those patients who experience difficulty in reducing their benzodiazepine use due to withdrawal symptoms, substitution with an equivalent dose of a longer acting benzodiazepine such as diazepam may be necessary. Dose equivalents of the commonly used benzodiazepines are presented in Table 2.4.3.

Occasionally, it may be necessary to withdraw hospitalised patients abusing high doses of benzodiazepines. Conversion of the benzodiazepine medication the patient was taking into

an equivalent dose of diazepam should be carried out, with the consent of the patient. On the first day of the benzodiazepine withdrawal programme, the patient should be given 40% of the usual daily dose in 3 equally divided doses. Thereafter, reduce dosage by 10% per day if symptoms are reasonably well controlled.

It is recommended that patients receive regular follow up for at least one month after cessation of the medication, in order to continue monitoring their health and provision of support.

Table 2.4.3

Dose Equivalents of Commonly Available Oral Benzodiazepines.

Diazepam 5.0mg is equivalent to	Chlordiazepoxide	25.0mg
	Lorazepam	1.0mg
	Oxazepam	30.0mg
	Temazepam	20.0mg
	Nitrazepam	2.5mg
	Flunitrazepam	1.0mg
	Bromazepam	3.0mg
	Alprazolam	0.25mg
	Triazolam	0.5mg

2.4.6 Alternatives to benzodiazepine treatment

Exposure of patients and hospital staff to an educational intervention designed to increase understanding of insomnia, promote appropriate drug use and prescribing and encourage the use of non-pharmacological methods to aid sleep, can be effective in reducing the number of patients taking hypnotic medications after discharge (Carey, Day, Cairns et al., 1992).

Non-pharmacological management for anxiety and insomnia requires clarification of the problem and simple counselling, with advice and reassurance. Patients may also benefit from provision of information sheets specific to their problem, including relaxation techniques, structured problem solving and hints for better sleeping habits.

Patients may also benefit from referral to specialist practitioners and/or support organisations.

2.4.7 Conclusion

Benzodiazepines are relatively safe medications with few side effects, unless taken with other drugs. However, for most patients, prescribing of benzodiazepines for periods greater than 2 to 4 weeks is not recommended, due to the dependence and withdrawal potential of these medications. Caution must be exercised when prescribing benzodiazepines for individuals with a previous history of drug or benzodiazepine dependence, benzodiazepine withdrawal, patients with maladaptive personality styles and the elderly.

The substantial cohort of long term users of benzodiazepines, especially for insomnia, highlights the need for better education of the public and the medical profession about sleep disorders.

Overall, the elderly and female consumers are the major users of benzodiazepines. The elderly, and in particular elderly women, have an increased likelihood of using multiple medications (Simons, Tett, Simons et al., 1992). Thus, medication review is advisable.

2.4.8 References/additional reading

Ames D. 'Safe hypnotic use in the elderly'. Current Therapeutics, 32, 1991, p57.

Australian Bureau of Statistics, 1991. 'Australian Health Study 1989-1990'.

Busto U, Sellers E, Naranjo C et al. 'Withdrawal reaction after long term therapeutic use of benzodiazepines'. N Engl J Med, 315, 1986, p854.

Berry GC. 'Sleep and hypnosedative use in the elderly'. Modern Medicine, Oct 1990, p70.

Carey DL, Day RO, Cairns DR et al. 'An attempt to influence hypnotic and sedative drug use'. Med J Aust, 156, 1992, p389.

Gaudreault P, Guay J, Thivierge RL et al. 'Benzodiazepine poisoning. Clinical considerations and treatment'. Current Therapeutics, 1992, 33, p85.

Foy A, Drinkwater V, March S et al. 'Confusion after admission to hospital in elderly patients using benzodiazepines'. BMJ, 293, 1987, p1072.

Ghodse H & Khan I. 'Psychoactive drugs: Improving prescribing practices'. World Health Organisation, Geneva, 1988.

Jacobson GA, Triesen WT, Peterson GM et al. 'Psychoactive drug prescribing in the Tasmanian community'. Med J Aust, 157, 1992, p20.

Mant A, Whicker SD, Birkett DJ et al. 'Benzodiazepine utilisation in Australia with international comparisons'. (Submitted for publication).

Mitchell P & Mant A. 'Insomnia'. Med J Aust, 154, 1991, p 193.

'NH & MRC Guidelines for the prevention and management of benzodiazepine dependence'. Monograph series No. 3.

Victorian Medical Postgraduate Foundation. 'Psychotropic drug guidelines', 1st edition, 1989/90.

Table 2.5.1

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Available by Prescription in Australia

Drug	Trade names
Aspirin	Ecotrin; SRA; ASA
Diclofenac	Voltaren
Diflunisal	Dolobid
Ibuprofen	Brufen; Inflam; Rafen
Indomethacin	Indocid; Arthrexin; Rheumacin
Ketoprofen	Orudis; Orudis SR
Naproxen	Naprosyn; Naxen
Phenylbutazone	Butazolidin
Piroxicam	Feline
Sulindac	Clinoril
Tenoxicam	Tilcotil

NSAIDs differ widely in chemical structure, and therefore physiochemical properties, and it is these differences between the NSAIDs' physiochemical properties which result in differences in preferential sites of action, duration of action and adverse effects. Acidic NSAIDs are preferentially sequestered in synovial tissue, and are therefore present at or close to the site of inflammation, which may be beneficial for the treatment of some patients. The more lipid soluble the NSAID, the greater the likelihood of central nervous system effects, especially in the elderly.

NSAIDs are readily absorbed after oral administration, are highly bound to plasma albumin and undergo hepatic and renal metabolism and excretion. Time for onset of action after oral administration is similar for all NSAIDs. Plasma half-lives of prescribed NSAIDs range from 0.25 hours for aspirin to 68 hours for phenylbutazone. However, dosing schedules, and thus the effectiveness of the NSAIDs, do not correlate with the respective half-lives, possibly in part because of the diffusion rate of the drug into the synovium. Unlike other NSAIDs, the hepatic metabolism of aspirin and sulindac produces active metabolites with anti-inflammatory actions. Inactive acyl glucuronide metabolites of some NSAIDs, which undergo renal elimination, may be retained and converted back into the active parent compound in patients with impaired renal function, thereby increasing levels of active NSAID and increasing the risk of toxicity.

Generally, the lowest dose of NSAIDs produces most of their antiinflammatory response. In the event of insufficient clinical effect, titration of dose against symptoms should be effective in overcoming the wide intersubject variation in response to NSAIDs. Should the patient remain unresponsive to a specific NSAID after two weeks of therapy, an

alternative NSAID should be trialled. Two or more NSAIDs should not be administered concurrently, as the drug effects are not additive or synergistic.

For further details see Day, 1990; Johnson & Day, 1991a.

2.5.4 NSAIDs in the treatment of musculoskeletal pain

Relief from musculoskeletal pain is often dependent on the diagnosis of the nature of the pain. Much musculoskeletal pain is transient and responds to rest, heat or exercise. Treatment is determined by the type, cause and severity of the pain. Therapeutic options for overall management of musculoskeletal pain include physical, medication including NSAIDs and surgery.

*** Osteoarthritis**

The aetiology of osteoarthritis is multifactorial, with ageing, mechanical, genetic and cultural factors all contributing to the development of joint failure. Clinically, the disorder is characterised by crepitus, pain, deformity and limitations of movement. The intensity of pain experienced will fluctuate, especially with physical exercise.

NSAIDs are widely prescribed, and are effective in the symptomatic relief of pain. However, reliance on this type of pharmacological management alone is questionable, due to the adverse effects of these drugs, particularly in the elderly. Also, there is very little evidence which supports the provision of any beneficial anti-inflammatory role of NSAIDs long term in osteoarthritis. Several studies have failed to demonstrate increased pain relief in osteoarthritis with NSAIDs, at analgesic or the larger anti-inflammatory doses, when compared with paracetamol. Thus, current management of osteoarthritis does not recommend NSAIDs as the first line of management. Rather, NSAIDs should only be prescribed when paracetamol does not provide adequate pain relief. To keep the NSAID intake at the lowest effective dose, the NSAID can be prescribed in combination with paracetamol.

Optimal management of osteoarthritis requires individualised therapy and regular patient review. Management should be directed at protection from mechanical abuse of the involved joint(s) in conjunction with pain control. Weight reduction and improved fitness, gained by an exercise programme designed specifically for the patient (See Section 2.5.7), are important aspects of the non-pharmacological management of osteoarthritis and other musculoskeletal disorders. Patients should also be educated in the management of analgesic medication intake for pain when necessary, rather than NSAID administration on a continuous basis.

For further details see Bradley, Brandt, Kate et al., 1991; Day, Seideman & Cohen, 1992; Pinals, 1992.

* Rheumatoid arthritis

Rheumatoid arthritis is a chronic multisystem disease of unknown aetiology. The characteristic feature of rheumatoid arthritis is persistent inflammatory synovitis, generally involving peripheral joints. Persistent inflammation leads to cartilage destruction, erosion of bone and joint deformities. Rheumatoid arthritis affects approximately 1% of all adult populations. Females are affected three times more than males. Prevalence increases with age. Family studies indicate a genetic predisposition.

Early diagnosis and treatment of rheumatoid arthritis is important to prevent joint destruction. Treatment aims to provide relief from pain, reduce inflammation, maintain joint and muscle function, thereby improving the patient's quality of life. To achieve each of these treatment aims, individualised management programmes must be devised in conjunction with the patient, as discussed previously for the optimal management of osteoarthritis.

First line agents for the management of active rheumatoid arthritis are NSAIDs. Analgesia from paracetamol alone is often unsuitable, however combinations of an NSAID agent and paracetamol may provide suitable pain relief, thus keeping the NSAID dose lower than if taken alone. NSAIDs in combination with low dose antidepressants may result in greater relief from pain in some patients.

For further details see Day, 1990; Zilko, 1990; Egger, 1991; Arnold, Sonnabend & Schreiber, 1992; Australian Gastroenterology Institute, Arthritis Foundation of Australia and Australian Rheumatology Association, 1992.

* Juvenile chronic arthritis

Juvenile chronic arthritis affects only 0.1% of children under 16 years of age. The overall prognosis of the disease is good, with 40% of children having no residual disability and 30% experiencing minor problems.

Therapy aims to prevent joint deformity and maintain joint and muscle function, whilst allowing the patient to maintain a reasonable quality of life. As for the treatment of adult osteoarthritis and rheumatoid arthritis, individualised programmes consisting of physical, social, occupational, psychological, educational and pharmacological components are required for optimum management of the disease. These programmes should involve family members as well as the patient and associated medical staff.

NSAIDs are usually the only drugs required in the treatment of juvenile chronic arthritis. NSAIDs recommended for use in children with juvenile arthritis include ibuprofen, naproxen, diclofenac, indomethacin and piroxicam. Aspirin use is contraindicated in children or adolescents, due to a strong association of aspirin intake and the hepatotoxic Reye's syndrome.

For further details see Rudge, 1990.

* Gouty arthritis

Gouty arthritis generally occurs in conjunction with raised uric acid levels. Crystal formation of monosodium urate may precipitate an acute inflammatory response in the synovium. NSAIDs are the drug of choice for acute gouty arthritis and provide pain relief within 4-6 hours, when given orally and in adequate dosage. Failure to resolve symptoms within 24 hours on the prescribed NSAID requires an alteration in drug therapy. Aspirin should be avoided in the treatment of gout, as it may raise uric acid levels. Urate-lowering medication should not be introduced, or dosages increased, until the acute attack has completely passed. For further details see Bellamy & Brooks, 1990.

* NSAIDs in the treatment of dysmenorrhea

Dysmenorrhea is associated with increased prostaglandin F2a. Due to their inhibition of prostaglandin synthesis, therefore, NSAIDs may be effective in the symptom and pain control of dysmenorrhea. NSAIDs commonly prescribed for dysmenorrhea include aspirin, naproxen sodium and mefenamic acid. In conjunction with inhibition of prostaglandin synthesis, mefenamic acid also antagonises prostaglandin receptors which may contribute to its role in the treatment of dysmenorrhea.

2.5.5 Adverse effects and possible drug interactions

The most frequently reported problems to NSAIDs are:

* Gastrointestinal

Dyspepsia (indigestion, heart burn and nausea) is reported in 10-15% of patients taking NSAIDs. Inhibition of the prostaglandins in the gastric mucosa is attributed to these gastrointestinal disturbances. Newer NSAIDs, the development of enteric coated preparations, administration of medication with or after food, or with an antacid preparation, contribute to a reduced incidence of gastrointestinal effects.

Peptic ulceration is less common than dyspepsia (see Section 2.5.1). Non-aspirin NSAIDs cause significantly less

gastrointestinal damage than aspirin. An increased high risk of NSAID-induced peptic ulcer complication can be expected in the elderly and in patients with a history of gastric ulcers or bleeds, use of antacids or H2-antagonists, corticosteroids or cigarette smoking.

Treatment for gastroduodenal complications includes antacids and H2-antagonist therapy. Misoprostol, a prostaglandin analogue, is reported to successfully heal NSAID-induced gastroduodenal lesions and to prevent the recurrence of gastric lesions in the presence of ongoing NSAID treatment. Recent evidence supports the cost-effectiveness of misoprostol for the first three months of NSAID therapy in patients who require chronic NSAID administration and are at risk of gastrointestinal toxicity.

For further detail see Day, 1991; Elliott, 1991.

* Renal

NSAIDs can produce or aggravate a wide range of renal syndromes. NSAID inhibition of synthesis of the prostaglandins necessary for the maintenance of renal blood flow may reduce glomerular filtration rate and renal blood flow, which with chronic NSAID use progresses to renal impairment. Risk factors contributing to NSAID-induced toxicity include: the NSAID involved, dose, duration of therapy, age, concurrent diseases and medications and preexisting renal disease. For further detail see Hoitsma, Wetzels & Koene, 1992.

* Hepatic

Liver damage has been reported for most of the NSAIDs available, however aspirin and phenylbutazone are the only NSAIDs attributed with direct toxic effects on hepatic tissue. In the event of hepatotoxicity, the medication should be withdrawn and NSAIDs from the same class should not be prescribed.

* Neurological

Mood swings, behavioural disturbances, confusion, perceptual dysfunction and dizziness have all been attributed to NSAIDs. The lipophilic nature of the NSAID is thought to be the factor contributing to NSAID-induced neurotoxicity.

* Dermatological

Cutaneous adverse reactions to NSAIDs range from mild to severe urticaria, rashes, purpura, cutaneous vasculitis, photosensitivity, Stevens-Johnson syndrome and toxic epidermal necrosis. In Australia, the highest rate of photosensitivity reactions reported for NSAIDs correlated with those NSAIDs most frequently prescribed: naproxen, sulindac, diclofenac and diflunisal.

* **Haematological**

NSAID-induced bone marrow suppression is rare, and those agents responsible (phenylbutazone and oxyphenbutazone) have been withdrawn from general use.

Irreversible inhibition of prostaglandin synthesis results in reduced platelet adhesives and prolonged bleeding times induced by aspirin, which may pose a surgical problem. However, patients with thromboembolic risk factors benefit from this effect of aspirin, when it is administered in lower doses.

* **Some of the important NSAIDs/other drug interactions are with:**

Oral anticoagulants - possible increase of anticoagulant effect, due to increased concentrations of free anticoagulants.

Lithium - reduced excretion of lithium increases risk of toxicity.

Oral hypoglycaemics - reduced metabolism of hypoglycaemic agent increases the risk of hypoglycaemia.

Digoxin - increased digoxin levels and toxicity risk, due to reduced renal clearance.

Antihypertensives - reduced hypotensive effects, due to altered renal function.

For further details see Day, 1990; Johnson & Day, 1991; Australian Gastroenterology Institute, Arthritis Foundation of Australia and Australian Rheumatology Association, 1992.

2.5.6 Prescribing NSAIDs for the elderly

Medication review is advisable prior to prescribing any medication, in order to avoid duplication of current medications in use and possible drug interactions. Due to possible pharmacokinetic and pharmacodynamic changes associated with ageing, the increased likelihood of multiple medication use in these patients, the need for NSAIDs, the choice of NSAID and the duration of therapy must be carefully considered, in an effort to avoid drug interactions and adverse effects.

Recommendations for optimum management of the elderly patient requiring NSAIDs include regular clinical assessment - blood pressure measurement, full blood counts, renal and hepatic function tests - which should be carried out to monitor patient progress and the possible need for continuation of therapy. Sources of important interactions of NSAIDs with other medications are as previously discussed (see Section

2.7.5), however the likelihood of such interactions occurring is raised in the elderly.

For further information on specific drug interactions and adverse effects, see Johnson & Day, 1991.

2.5.7 Non-pharmacological support strategies

Non-pharmacological support strategies for musculoskeletal conditions often include physiotherapy, physical exercise, good nutritional management, occupational therapy and education. All contribute to an improved quality of life for the patient.

Physiotherapy programmes aim to improve muscle strength and length, improve joint function and to educate the patients in the overall management of their condition. Exercises, heat, cold, rest, splinting, soft tissue massage, joint mobilisation, orthotic devices, walking aids and transcutaneous nerve stimulation for pain relief may all be involved. Hydrotherapy can play a major role in the management of patients with advanced disabilities or involvement of weight bearing joints.

Exercise suitable for arthritis patients includes swimming, aquarobics, low impact aerobics, walking and light weight training. Strengthening of joints can help to reduce immobilisation and reverse deteriorating co-ordination effects.

Little evidence is available which supports anything other than good nutritional management (high fibre intake from fruits, vegetables and complex carbohydrates; dairy products; low intake of saturated fats), including adequate vitamin, mineral and calcium intake for patients with rheumatic diseases. Benefits from marine oils are limited, particularly when compared to the large quantities of marine oil necessary to produce such benefits. Control of serum uric acid levels in patients with gout is seldom achieved by reduction of intake of purine-containing foods without the addition of a uric-acid-lowering medication. However, restriction of purine intake does reduce the dose requirements of uric-acid-lowering medications required.

Education of patients provides reassurance, as well as promoting a greater understanding of their arthritic complaint. In turn, patient compliance to management regimens may be improved and overall improve the patient's quality of life. Patient education may be provided by all health professionals with whom the patient interacts and support organisations which specifically deal with the disorder, such as the Arthritis Foundation of Australia.

For further details see Howe, 1990; Bellamy & Brooks, 1991; Egger, 1991; Morand, 1991.

2.5.8 Conclusion

The prescribing and/or use of NSAIDs is often inappropriate. NSAIDs are most effective in disorders with inflammatory components. Two or more NSAIDs should not be given concurrently as effectiveness is unaltered and the risk of NSAID-induced adverse effects increased. Non-pharmacological therapy often aids management of the underlying condition, and may lead to a reduction in medication intake and a better quality of life for the patient. Medication and clinical progress reviews should take place regularly, particularly in the elderly and/or those patients on multiple medications.

2.5.8 References/additional reading

Ahern MJ & Rischmueller M. 'Problems of age in Rheumatology'. Modern Medicine, 35(7), 1992, p94.

Arnold MH, Sonnabend DH & Schreiber L. 'Current management of rheumatoid arthritis'. Modern Medicine, 35(2), 1992, p30.

Australian Bureau of Statistics, 1991. 'Summary results of the Australian National Health Survey, 1989-1990'.

Australian Gastroenterology Institute, Arthritis Foundation of Australia and Australian Rheumatology Association. 'Nonsteroidal anti-inflammatory drugs (NSAIDs) and the upper gut'. Modern Medicine, 35(7), 1992, p105.

Bradley JD, Brandt KD, Katz BP et al. 'Comparison of an anti-inflammatory dose of ibuprofen, an analgesic dose of ibuprofen, and acetaminophen in the treatment of patients with osteoarthritis of the knee'. N Engl J Med, 325, 1991, p87.

Bellamy N & Brooks PM. 'Gouty arthritis and hyperuricaemia: diagnosis and management'. Modern Medicine, 34(10), 1991, p53.

Brooks PM & Day RO. 'Nonsteroidal antiinflammatory drugs - differences and similarities'. N Engl J Med, 324, 1991, p1716.

Day R. 'Nonsteroidal anti-inflammatory drugs'. Modern Medicine, 35(6), 1990, p92.

Day R. 'Do anti-ulcer drugs prevent gastrointestinal damage from NSAIDs?'. Australian Prescriber, 14(3), 1991, p42.

Day R, Seidman P & Cohen M. 'Osteoarthritis. Current pharmacological management'. Current Therapeutics, 33(9), 1992, p29.

Elliott SL. 'NSAID gastropathy and the role of misoprostol'. Current Therapeutics, 32(8), 1991, p37.

Egger G. 'Prescribing exercise. Part 2: patients with special medical conditions'. Modern Medicine, 34(7), 1991, p106.

Gosh P. 'Osteoarthritis: aetiopathogenesis and management'. Modern Medicine, 34(8), 1991, p68.

Hoitsma AJ, Wetzels JFM & Koene RAP. 'Drug-induced nephrotoxicity'. Current Therapeutics, 33(2), 1992, p51.

Howe G. 'Physical therapy in rheumatic diseases'. Modern Medicine, 33(11), 1990, p73.

Johnson AJ & Day RO. 'The problems and pitfalls of NSAID therapy in the elderly (part 1)'. Drugs & Aging, 1(2), 1991a, p130.

Johnson AJ & Day RO. 'The problems and pitfalls of NSAID therapy in the elderly (part 2)'. Drugs & Aging, 1(3), 1991b, p212.

Jones AC & Doherty M. 'The treatment of osteoarthritis'. Br J Clin Pharmacol, 33, 1992, p357.

Morand EF & Littlejohn GO. 'Nutrition and rheumatic disease'. Modern Medicine, 34(8), 1991, p83.

Rudge S. 'Joint pains in children: assessing the serious causes'. Modern Medicine, 33(5), 1990, p113.

Shenstone B. & Fleming A. 'Management of musculoskeletal pain'. Modern Medicine, 33(3), 1990, p92.

Victorian Drug Usage Advisory Committee & Victorian Medical Postgraduate Foundation. 'Analgesic guidelines'. 1992.

Zilko PJ. 'Rheumatoid arthritis: diagnosis and management'. Modern Medicine, 33(9), 1990, p18.

2.6 Lipid lowering drugs

2.6.1 Introduction

Coronary heart disease (CHD) is the cause of almost 50% of all deaths per annum in Australia, i.e. more than 10,000 Australians less than 70 years of age.

The National Heart Foundation Risk Prevalence Survey recently demonstrated that, of the men and women surveyed, 47% and 39% respectively had elevated blood cholesterol levels in >5.5 mm/L. Similar results were demonstrated in a large-scale community-based cholesterol screening programme on the North Coast of NSW (van Beurden, James, Henrickson et al., 1991).

There is considerable evidence which demonstrates the relationship of raised serum cholesterol levels (hyperlipidaemia) with development and progression of atherosclerosis and subsequent coronary heart disease (CHD). Prevention of heart disease in these patients is associated with reduction of plasma lipids, through dietary therapy alone or through dietary and drug therapy in combination. For each 1% reduction in total blood cholesterol level, a 2-3% reduction in risk of CHD can be anticipated.

Hypercholesterolaemia is related to raised blood levels of lipid complexes responsible for transportation of cholesterol in plasma. Low density lipoprotein (LDL) has a clearly defined role in the genesis of coronary heart disease. LDL is the principle lipoprotein for cholesterol transport in the blood, therefore reduction of LDL levels will result in a significant lowering of cholesterol levels. High density lipoprotein (HDL) transports cholesterol from peripheral tissues and vasculature to the liver for breakdown and elimination. Thus, HDL is important in maintaining reduced levels of cholesterol, thereby reducing the likelihood of deposition of cholesterol-related atherosclerotic plaque. High levels of HDL have been associated with reduced risk of CHD. Hypertriglyceridaemia is due to an excess of very low density lipoprotein (VLDL). VLDL is a precursor of the LDL fraction, and has a cholesterol component incorporated with the triglycerides. Reduction of VLDL formation will lower both serum triglyceride and cholesterol levels.

Acceptable levels of serum lipids are:

- total cholesterol of <5.5 mmol/L
- low density lipoprotein level (LDL) of <3.5 mm/L
- high density lipoprotein level (HDL) >0.9 mm/L and
- a triglyceride level of <2.00 mm/L.

Risk factor management is as important in patients after surgical revascularisation or angioplasty as it is for those patients newly diagnosed with hyperlipidaemia. Lipid control for these patients should be stricter and aiming for a total cholesterol <4.5 mm/L, LDL <2.7 mm/L, HDL >1.5 mm/L.

Lipid reduction can be achieved by non-pharmacological and pharmacological means. However, before designing a management plan for the patient, the risk factors for CHD must be considered.

For further details see Beilin et al., 1992; Goldman, Gordon & Rifkind, 1992; LaRosa & Cleeman, 1992.

2.6.2 Risk factors for CHD

Determination of medical management of the hyperlipidaemic patient is influenced by serum lipid profiles in association with:

*** History of cardiovascular disease**

Changes in underlying pathology from previous cardiovascular events predisposes these patients to a further cardiovascular events.

*** Age**

Vascular disease increase with age.

*** Sex**

Vascular disease is predominantly a male health problem until the sixth and seventh decades of life, when female rates of vascular disease increase and almost equal that for males. It is possible that hormonal changes associated with menopause may be a major contributing factor to this change in risk rate.

*** Cigarette smoking**

Smoking increases the risk of CHD, with direct changes to the vasculature in conjunction with altered blood clotting and lipid profiles. Smoking also reduces the therapeutic effects of lipid-lowering and antihypertensive medications. All patients should be advised of the major benefits of cessation of smoking on their risk of CHD. Nicotine gum or specialised counselling (individual or group) may also be useful in providing motivation and/or reinforcement for a change in smoking behaviour.

*** Obesity**

Obesity is associated with a high risk of vascular mortality and morbidity. Obesity may be due to excessive eating, reduced physical activity, excessive alcohol intake, diabetes mellitus, genetic background or a combination of all of these factors. Evidence suggests that gynoid or abdominal obesity does present a higher risk of CHD than android obesity. Introduction of the lipid lowering diet (see Section 2.6.5), in conjunction with increased physical activity, should reduce this risk factor.

* **Physical activity**

Evidence suggests that physically active individuals have a lower risk rate of coronary heart disease than individuals who are inactive. Regular physical exercise in conjunction with low fat diets alone has been demonstrated to slow down the progression rate of coronary artery disease. Weight loss, or maintenance of attained body weight, and body shape are also attributed to by regular physical activity, although recent investigations suggest that the relationship between exercise and biological CHD risk factors (blood pressure and serum cholesterol and triglycerides) is only slight.

* **Hypertension**

The contributions of hypertension to vascular disease, and thus CHD, are well documented. Treatment of hypertension should not be managed on drug therapy alone. Overall management should also include life-style management, including weight control, serum lipids and physical activity. Increased management of these factors, in conjunction with antihypertensive drug therapy, may then reduce the risk of CHD in these patients.

* **Diabetes mellitus**

Changes in carbohydrate metabolism contribute directly to vascular disease, and atherosclerosis may be further aggravated with increased lipid levels.

* **Family history of CHD**

The incidence of cardiovascular disease in a first degree relative younger than 60 years of age increases the risk of CHD.

For further details see Powell, Thompson & Caspersen, 1987; Poulter, 1990; Bauman & Owen, 1991; Baur, 1992; Schuker, Hambrecht, Schlierf et al., 1992.

2.6.3 Pharmacology of lipid lowering drugs

Drugs used for the lowering of plasma lipids either decrease the amount of lipid entering the plasma or increase the rate of clearance of lipids from the plasma.

* **HMG-CoA reductase Inhibitors**

Simvastatin, a HMG-CoA reductase inhibitor, suppresses the synthesis of cholesterol in the liver, thereby increasing cellular requirements for the uptake of plasma cholesterol. Up-regulation (increase in receptor number) of LDL receptors on the cell membrane facilitates increased cellular uptake of plasma LDL and also entrapment of LDL, thereby contributing to reduced levels of cholesterol and triglycerides.

Simvastatin is useful in lowering cholesterol levels in heterozygous familial hypercholesterolaemia (FH). Before commencement of simvastatin therapy, LDL receptor number is about half that of normal individuals, which results in cholesterol levels 2-3 times greater than average.

Simvastatin is not recommended for prescribing to pregnant women or children with hyperlipidaemia, or in combination with fibrates or nicotinic acid.

* Bile acid resins

Cholestyramine and colestipol exchange chloride for anions and bind bile salts within the intestinal lumen. Reduced levels of available bile salts initiate a feedback mechanism responsible for increased conversion of cholesterol to bile salts, thereby resulting in reduced cholesterol levels.

Ion exchange or bile acid resins are capable of binding to many orally administered drugs, thereby reducing bioavailability of the administered drugs. Thus, other medications should never be taken in conjunction with these resins. Dosing with other medication should be several hours before or after ingestion of the resin.

These drugs must be prescribed with caution in patients with lower bowel disease.

* Fibrinic acid derivatives

Gemfibrozil inhibits the synthesis of VLDL and enhances its clearance from the plasma, thus reducing triglyceride and cholesterol levels. Breakdown of the VLDL particles increases the formation of HDL.

* Nicotinic acid

Nicotinic acid (vitamin B3 or niacin) is thought to inhibit the mobilisation of free fatty acids necessary for triglyceride production. Reduced triglyceride production also lowers VLDL production, thereby bringing about reduction of LDL.

Nicotinic acid should be prescribed with caution in patients with diabetes and liver disease, as it may interfere with glucose tolerance and hepatic function.

Avoid prescribing with simvastatin, due to an increased risk of myopathic reaction.

* Probucil

Probucil is postulated to alter the structure of the LDL particle, which results in a more rapid clearance of LDL from the plasma. This drug is also attributed with antioxidant properties which inhibit the oxidative mechanism responsible for atherosclerotic plaque formation in the vasculature.

Administration of probucil with fibrinic acid derivatives is not recommended due to the possibility of a marked lowering of HDL levels.

For further details see Fidge, 1990; Simons, 1990, 1991 & 1992; Jamus, 1991.

2.6.4 Adverse drug effects

*** HMG-CoA reductase inhibitors**

Headache, fatigue and gastrointestinal disturbances.

Minor elevations of liver transaminases, which are usually transient and do not require withdrawal of therapy. Liver function tests should be performed regularly.

Mild elevations in plasma creatine kinase and myopathy have occurred in some patients. However, myopathy has mainly been associated with combination drug therapy. Musculoskeletal pain occurs in 2-3% of patients taking simvastatin, and withdrawal of the medication is usually necessary.

Ocular damage has been described in experimental trial animals treated with simvastatin, therefore patients should have regular ophthalmic examinations and should inform the clinician of any irregularities in vision.

*** Bile acid resins**

Gastrointestinal disturbances, including severe constipation or steatorrhea, due to binding of fatty acids.

*** Fibrinic acid derivatives**

Gastrointestinal disturbances. Increased concentrations of cholesterol in bile may precipitate gallstones.

*** Nicotinic acid**

Cutaneous flushing and itching are the main side effects. Gastrointestinal irritation, which may be reduced if medication is taken with food.

*** Probucol**

Gastrointestinal disturbances.

For further details see Simons, 1990, 1991 & 1992; Jamus, 1991.

2.6.5 Lipid lowering dietary treatment

Dietary treatment with a low fat/high fibre (including soluble fibre - oat and wheat bran) and high complex

carbohydrate cholesterol-lowering plan, as recommended by the National Heart Foundation, should be the first line of therapy for all hyperlipidaemic patients. Thus, current dietary treatment for lipid-lowering management advises a daily food intake, where less than 30% of total calories is as fat and less than 10% is saturated fat. Suggested alcohol intake should be moderate (2 standard drinks = 20g/day) and binge drinking should be avoided.

Patients should be encouraged that dietary treatment is a life long contribution to the overall management of their CHD. A lipid-lowering diet alone may be successful in lowering lipoprotein levels to the recommended total cholesterol levels of <5.5 mm/L. Marked changes in serum lipid profile should be demonstrated in 6 to 8 weeks of dietary manipulation, with a 10-20% reduction in serum cholesterol levels.

As a general rule, the lipid-lowering diet should be continued for six months, when after further measurement of the serum lipid profile, a decision regarding the possible incorporation of drug therapy into lipid-lowering management is made and a management plan designed.

Drug therapy should only be introduced in less than six months to those patients with:

- very high triglyceride levels (>12mm/L) who have failed to respond to abstinence from alcohol and dietary measures.
- familial hypercholesterolaemia
- recent coronary artery bypass grafts
- multiple risk factors.

2.6.6 Management with lipid-lowering diet and drug treatment

Lipid-lowering drugs should be introduced after six months' compliance with dietary therapy in the following situations:

*** Hyperlipidaemia**

Hyperlipidaemia in the absence of other cardiovascular risk factors, with a serum lipid profile of a total cholesterol of >7.5 mm/L and an HDL level of approximately 1.5mm/L. Patients with a total cholesterol <7.5 mm/L, in conjunction with a low HDL level, should be considered for drug therapy.

Drug treatment

Simvastatin, a HMG-CoA reductase inhibitor, is effective in reducing cholesterol and triglyceride levels and raising HDL. Simvastatin is more easily tolerated in patients than other lipid-lowering medications. Medication review should be carried out 6 weeks after commencement of simvastatin. Dose titration may be required with increasing doses.

For resistant cases, simvastatin can be combined with a resin agent to reduce cholesterol levels.

* **Hypertriglyceridaemia**

Hypertriglyceridaemia with low HDL cholesterol levels should be reviewed with respect to lifestyle factors - diet, weight, exercise and alcohol. Drug therapy is recommended with triglyceride levels of $>4.0\text{mm/L}$ and an HDL of level 0.9mm/L after life-style changes (dietary and alcohol) have been implemented by the patient. However, the continuing presence of risk factors - obesity, poor glycaemic control or excessive alcohol intake may negate beneficial effects of drug therapy.

The risk of pancreatitis is raised if triglyceride level remains $>8.0\text{mm/L}$, even after accounting for alcohol intake.

Drug treatment

Gemfibrozil may be used to commence treatment and progress assessed at 6-8 weeks. Fish oils may lower triglyceride levels via production of VLDL triglycerides. Nicotinic acid may be used alone or in combination with gemfibrozil for resistant cases.

* **Mixed hyperlipidaemia**

Lipid-lowering medication may be appropriate in patients with hypercholesterolaemia (total cholesterol $>6.5\text{mm/L}$, with an HDL level of approximately 1.5mm/L) together with any other cardiovascular risk factor - smoking, high blood pressure, diabetes mellitus, family history of premature cardiovascular disease.

Raised HDL levels may contribute to raised cholesterol levels and therefore drug therapy may be inappropriate. However, if HDL levels are very low, then drug therapy should commence at lower levels of total cholesterol.

Patients with hyperlipidaemia and existing heart disease should be considered for drug therapy, when total cholesterol remains greater than 6.5mm/L . However, for those patients with a high risk of further coronary events, especially patients with recent coronary revascularisation, coronary angioplasty and peripheral vascular surgery, a total cholesterol level $<6.5\text{mm/L}$ may be considered for introduction of lipid lowering drugs.

Drug treatment

Simvastatin may be effective if hypercholesterolaemia predominates. Gemfibrozil may lower cholesterol and triglyceride levels and increase HDL levels. Nicotinic acid alone may reduce both cholesterol and triglyceride levels, or in combination with a bile acid resin medication.

Caution must be exhibited with combinations of lipid-lowering drugs until data are available from trials with greater numbers of patients with prolonged use of combination lipid lowering medication.

Duration of drug therapy in conjunction with dietary therapy for management of lipid levels is generally considered to be life long. With cessation of medication or diet, serum lipid levels may increase. However, in patients who have maintained reduced serum lipid levels with medication and effective dietary and lifestyle changes for 2-3 years, withdrawal of dietary therapy can be trialled.

*** Indications for other uses of lipid-lowering medications**

Lipid lowering medications are also indicated for:

Pancreatitis due to hypertriglyceridaemia ($>8\text{mm/L}$)
Chronic diarrhoea following bowel resection may be managed with bile acid resins
Pruritis associated with partial biliary obstruction may be reduced with bile acid resins.

For further details see Simon, 1990; Benrimoj, Robinson & Stewart, 1991; Richards, 1991; Beilen, 1992.

2.6.7 Patient education

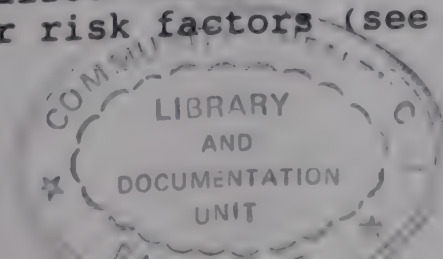
Establishment of a good relationship with each patient is an important factor in enhancing the therapeutic and educational potential of each consultation and thus overall management of the patient.

Effective health education requires personalising the management plan and therefore the interaction with each patient. To bring about change in lifestyle behaviours, the patients must be given the necessary information about health and each of the risk factors relevant to their management plan and this information should be reinforced. Motivation for changes in lifestyle must be given, realistic targets with respect to health goals should be set, and the development of skills necessary for attaining these goals by the patient encouraged. Maintenance of changes in lifestyle behaviours must be monitored regularly at followup.

For further details see Carroll, 1990.

2.6.8 Conclusion

Overwhelming evidence supports the benefits and cost-effectiveness of cholesterol-lowering management for prevention of death from coronary heart disease in high risk persons, i.e. those individuals with raised serum cholesterol and pre-existing CHD and/or other risk factors (see Section 2.6.2 and



2.6.6). In support of this evidence and information from the 1992 Consensus statement on the management of hyperlipidaemia, the most recent Pharmaceutical Benefits Scheme Guidelines have extended the subsidization of lipid-lowering medication for patients. Thus, if, after six months on a management plan incorporating stringent low fat diet requirements and reduction of other risk factors such as smoking and physical inactivity lipid levels are still raised, with a total cholesterol level $>6.5\text{mm/L}$ and/or triglyceride level 4.0mm/L , such a patient is entitled to subsidized lipid-lowering medication.

Current evidence also suggests that the benefits (i.e. number of deaths due to CHD prevented) of lipid-lowering medication to individuals with raised serum cholesterol levels and no evidence of CHD are not great enough to justify the expense incurred (Silberberg & Henry, 1991b). Neither is population screening of blood lipid levels considered justifiable, with respect to the expenses involved and the benefits to the individual of the knowledge of their blood cholesterol level (Jamrozik, 1991). However, all Australians should be encouraged to eat less fat because of its potential benefits for cardiovascular disease, obesity, diabetes mellitus and cancer.

2.6.9 References/additional reading

Beilin L et al. 'The management of hyperlipidaemia: a consensus statement'. Med J Aust, 156 (Supp), 1992, S1.

Bauman A & Owen N. 'Habitual physical exercise and cardiovascular risk factors'. Med J Aust, 154, 1991, p22.

Baur G. 'How to prevent vascular disease'. Modern Medicine, 35(4), 1992, p14.

Benrimoj SJ, Robinson MT & Stewart K. 'Drugs which lower cholesterol'. Australian Pharmacist, 10(4), 1991, p176.

Carroll A. 'Cardiovascular disease: the role of general practitioners in prevention'. Modern Medicine, 33(4), 1990, p96.

Fidge NH. 'Lipid-lowering drugs - mechanisms of action'. Australian Prescriber, 13, 1990, p73.

Goldman L, Gordon DJ, Rifkind BM et al. 'Cost and health implications of cholesterol lowering'. Circulation, 85, 1992, p1960.

Jamrozik KD. 'Cholesterol testing. Policy statement for the Australasian Epidemiological Association'. Med J Aust, 155, 1991, p495.

Janus ED. 'HMG-CoA reductase inhibitors. Therapy for hyperlipidaemias'. Current Therapeutics, 32(1), 1991, p34.

LaRosa JC & Cleeman J1. 'Cholesterol lowering as a treatment for established coronary heart disease'. Circulation, 85, 1992, p1229.

Lintott CJ, Scott RS, Sharpe N et al. 'Treatment of primary hypercholesterolaemia with simvastatin. New Zealand multicentre evaluation'. Med J Aust, 155, 1991, p433.

McBride PE & Davis JE. 'Cholesterol and cost-effectiveness. Implications for practice, policy and research'. Circulation, 85, 1992, p1939.

Poulter NR, Thom SMC & Sever PS. 'Preventing CHD: why treating is not enough'. Modern Medicine, 33(9), 1990, p44.

Powell KE, Thompson PD, Caspersen CJ et al. 'Physical activity and incidence of coronary heart disease'. Annu Rev Public Health, 8, 1987, p253.

Richards D. 'The management of coronary risk factors'. Modern Medicine, 34(9), 1991, p16.

Schuler G, Hambrecht R, Schlierf G et al. 'Regular exercise and low fat diet. Effects on the progression of coronary artery disease'. Circulation, 86, 1992, p1.

Silberberg JS & Henry D. 'The benefits of reducing cholesterol levels: the need to distinguish primary from secondary prevention. 1 A meta-analysis of cholesterol-lowering'. Med J Aust, 155, 1991a, p665.

Silberberg JS & Henry D. 'The benefits of reducing cholesterol levels: the need to distinguish primary from secondary prevention. 2 Implications for heart disease prevention in Australia'. Med J Aust, 155, 1991b, p670.

Simons LA. 'Lipid-lowering drugs - clinical applications'. Australian Prescriber, 13, 1990, p77.

Simons LA. 'Guidelines for the evaluation and management of hyperlipidaemia'. Modern Medicine, 34(4), 1991, p62.

Simons LA. 'Lipid-lowering drugs'. Current Therapeutics, 33(6), 1992, p27.

Van Beurden EK, James R, Henrickson D et al. 'The North Coast Cholesterol Check Campaign. Results of the first three years of a large-scale public screening programme'. Med J Aust, 154, 1991.

SECTION 3

3.1 Appropriate use of medication

Projects specific for:

3.1.1 The elderly

In the ten-year period 1986 to 1996, the number of Australians older than 65 years of age is estimated to rise from 1.68 to 2.22 million, an increase of 32%. The high incidence of polypharmacy alone presents a need for further research into appropriate use of medicines by the elderly. Consideration of other contributing factors such as altered physiological functioning - absorption, distribution, renal and hepatic excretion - and pre-existing disease states, increase the need for greater understanding of safe medication use and the role of non-drug therapies. Importantly, updated information of drug dosages specific to the elderly and with specific categories of medications is needed. Such information is limited as only recently has there been acknowledgement by clinical researchers (large government regulatory groups) as to the importance of altered handling in the elderly.

Further recommendations of projects promoting appropriate medication prescribing and use in this group are made in the recently released draft of the Report and recommendations for national policy action to improve the use of medications for and by the elderly (Marr 1992).

3.1.2 Individuals with spinal cord injuries, specifically those with paraplegia and quadraplegia

In Australia, approximately 7000 people are known to suffer from spinal cord injuries, and yet information on appropriate medication for and use by such individuals is limited. Although only a small group, the cost of multiple medications, in conjunction with repeated hospital admissions often requiring highly specialised care, would make a considerable contribution to the health care costs. The "out of pocket " costs report responsible for estimation of medication costs (per year) after PBS rebates to the consumer is to soon to be released. It is reported to underestimate by a factor of five the "out of pocket " costs for quadraplegic patients (personal communication with Australian Quadraplegic Association).

The intrusion of spinal cord injury on physiological functioning is often marked and may require constant medication in an effort to maintain bowel and/or bladder function. Medication may also be related to injury-induced changes to mood and sleeping habits.

Recent participation in a workshop on drug use - prescribed medications and socially used drugs - suggested a paucity in the information on appropriate medication made available or retained by such individuals. It is also possible that

therapeutic actions of the prescribed medications may be impaired by the concomitant use of socially used drugs, including alcohol (personal observation).

3.1.3 Non-English speaking background (NESB) communities

Comparison between the limited number of NESB studies investigating medication use in people of NESB is difficult, due to use of different community group small sample sizes, and actual sources of information e.g. "key informants" rather than individuals. Implementing studies of drug use and/or knowledge are difficult because of specific community attitudes towards the use of medication and the anonymity with respect to health care. Thus, access to these populations is often limited to workers of similar cultural background.

A recently completed literature review of drug and alcohol research amongst NESB communities in Australia (Spathopoulos & Bertram, 1991) highlights the issues of the lack of knowledge of levels of consumption, especially with respect to prescribed (Shaw, Hemming & Hobson, 1977) and OTC medicines and exacerbation of this situation with little information provided from patient - doctor communication and the lack of labelling medications in specific community languages.

Dissemination of written information in community languages is often limited, due to the low rate of literacy older individuals have in their own language. This point is highlighted in results for the Drug Offensive Campaign, in that although some campaign information was translated into ten community languages, the translated versions were not used. Thus, dissemination of information on appropriate medication use to such communities must take into account language abilities, access to the health care system as well as attitudes towards health and use of medicines in order to make the information appropriate for the specific community.

Available research on the use of prescribed drugs in NESB communities suggests higher use of minor analgesics in Vietnamese (males and females), Turkish, Greek (males and females) and Italian (female) communities (Trimboli & Ridoutt, 1987; Spathopoulos & Bertram, 1991). Investigation into the incidence of gastrointestinal disorders specific to analgesic use may provide further evidence of inappropriate use of analgesics in these communities.

Psychological aspects of health may also influence the use of medications in individuals of NESB. Adaption to a new culture and the possible alteration in social and employment status may be contributing factors to the mental health of such individuals, thereby influencing mood, coping strategies, sleep patterns, gastrointestinal disorders etc. all of which may be treated with medication.

Further impact on health care costs is from the number of older individuals of NESB communities. The portion of the aged population born in NESB countries was 13% in 1966 and is estimated to increase to 30% by 2006. Italians, followed by Greeks, have the largest groups in the 60 years and over population (Australian Institute of Multicultural Affairs, 1983).

3.1.4 References

Australian Institute of Multicultural Affairs (AIMA), 1973, p227.

Marr R. Draft- Report and recommendations for national policy action to improve the use of medications for and by the elderly, 1992.

Rowland. 'Midterm review of the aged care reform strategy'. Discussion paper No. 3, 1991.

Shaw J, Hemming MP, Hobson JD & Marty J. 'A comparison of English and non-english speaking outpatients comprehension of medications'. Aust J Hosp Pharm, 7, 1977, p116.

Sinnett P. 'Diagnosis, disease and drug therapy for the elderly patient'. Commonwealth Department of Community Services and Health, 1991.

Trimboli A & Ridoutt L. 'The drug use patterns of four ethnic communities'. NSW Department of Health (CEIDA): Sydney, 1987.

'The mental health problems of migrants: report from Six European countries'. World Health Organisation. Denmark.

THE QUALITY USE OF MEDICINES

LIST OF PAST REPORTS, INQUIRIES etc.

The following is a list of the major sources of evidence surrounding the quality use of medicines:

- . Public Service Board Review of Drug Evaluation Procedures (1987)
- . Joint Parliamentary Committee of Public Accounts (1988)
- . Health Targets and Implementation Committee (1988)
- . Department of Health Commissioned Report on Drug Education (1988)
- . Rational Drug Use Policy Task Force, Consumers' Health Forum (1989)
- . National Polypharmacy Taskforce and Conference, the Australian Council on the Ageing (ACOTA), (1990)
- . Department of Health Commissioned Report: Drug Use and the Elderly (1990)
- . Conference of Rational Prescribing: The Challenge for Medical Educators, the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) and the Consumers' Health Forum (1991)
- . Bureau of Industry Economics (Evaluation Report 11) on the Pharmaceutical Industry: Impediments and Opportunities (1991)
- . Trade Practices Commission Inquiry into Self-Regulation of Pharmaceutical Promotion (1991)
- . National Health Strategy Background Papers (1991-2)
- . House of Representatives Standing Committee on Community Affairs Inquiry into the Prescription and Supply of Drugs (1992)

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APPENDIX III

STRATEGY DEVELOPMENT FOR PROMOTING OPTIMAL USE OF PHARMACEUTICALS IN AUSTRALIA

PRINCIPLES OF BEHAVIOUR CHANGE AND HEALTH EDUCATION

Mary Hodge and Andrew Gilbert
November 1991

Background

The Pharmaceutical Health And the Rational use of Medicines (PHARM) Working Party was formed in June 1991 and is comprised of expertise drawn from all areas involved in the pharmaceutical field, including medicine, pharmacy, nursing, industry, the consumer movement and government. Its role is to provide independent advice regarding promotion of the quality use of medicinal drugs to the Pharmaceutical Benefits Scheme Education Program and the Department, through the Pharmaceutical Education Advisory Committee (PEAC).

Vision

Education is seen as the primary tool for achieving optimal use of medicines although PHARM is aware of other means such as incentives and sanctions. In developing and implementing strategies and innovative techniques to achieve its aims, PHARM believes that a partnership is required between:

- . those who prescribe drugs
- . those who dispense and facilitate their use
- . those who take or consider taking drugs
- . those who make the drugs
- . the Government who monitors safety and efficacy and provides equity of access to drugs in the public interest.

The membership of PHARM reflects this partnership.

Principles (cont.)

In developing an educational strategy, PHARM will try to identify:

- . what will empower consumers to use drugs well;
- . what will empower professional helpers (doctors, pharmacists, nurses, others) to help consumers do this;
- . what constitutes effective education;
- . what combination of information, skills and motivation will be effective for different groups and the diversity within these (ethnicity, socio-economic status etc.);
- . what will work in practice; and
- . what standards should apply and who should set them.

Aim

Our stated aim is to optimise the quality of medication use in Australia within the context of a national drug policy. Quality of use is one of four key elements in that policy. PHARM will develop an education strategy to achieve this aim and recommend the establishment of a long-term mechanism for continuing the promotion of quality use of pharmaceuticals.

Definition

Optimal use of medication requires:

- . an awareness of the part drugs play in treating illness and maintaining health;
- . knowledge sufficient to choose the most effective medication/s for the individual concerned taking into account their clinical condition, risk, benefit, dosage, length of treatment, cost, monitoring of effect and consideration of alternatives; and
- . information which enables individuals to use drugs correctly and safely.

PHARM endorses the following 1987 World Health Organisation definition of rational drug use:-

Drugs are often required for prevention, control and treatment of illness. When a drug is required, the "rational use of drugs demands that the appropriate drug be prescribed, that it be available at the right time at a price people can afford, that it be dispensed correctly, and that it be taken in the right dose at the right intervals and for the right length of time. The appropriate drug must be effective, and of acceptable quality and safety....The formulation and implementation by governments of a national drug policy are fundamental to ensure rational drug use."

Principles (cont.)

Outcomes

The definition assists in framing outcomes for the promotion of optimal medication use. It is important to recognise the distinctions between ideal, optimal and actual use. Ideal use may reflect the ethical/philosophical issues and scientific evidence which rightly inform the standards set. However, we need to give consideration to what is achievable in the context of the relevant target groups.

Whilst we can observe and measure actual practice and form judgements about its divergence from the ideal, we should define the point to which actual practice can be altered. This point should be one that is achievable taking into account the realities of the clinical practice of medicine. In deciding what constitutes achievable, it is important that the target group and their peers who set and monitor their standards, agree that the goals are desired and achievable. This latter goal reflects optimal medication use. It is important to define ideal and hold it as such. In time it may be possible to move optimal towards ideal. There are implications both for content and process in making these distinctions, and raises the question, "Does the WHO definition of rational use mean ideal or optimal?".

The measurement of outcomes of any attempt to influence current practice is a necessary part of this process. Such evaluation informs strategic planning as well as providing feedback for all involved in bringing about changes.

Outcomes for 'bottomline' issues such as health status, quality of life, reduction of iatrogenic morbidity and mortality and the issue of cost (economic, social and political) in achieving these can be defined. However, indicators for these and data sources for establishing a baseline and measuring changes in these indicators must be identified and should be considered (eg the Health Insurance Commission and the Australian Institute of Health). It is possible to describe more specific outcomes which measure the impact on various targets, for example drug groups causing particular problems, target groups within the community or particular diseases/clinical problems.

A programme or set of programmes must be evaluated for changes in health behaviour. Objectives must be set for each of the levels of outcome referred to above. To do this we need to be clear about the philosophies and principles that best inform the actions which one planned, as well as the issues that contribute to any current sub-optimal use of medication.

Principles (cont.)

Philosophy

There are a number of ethical and legal rights and obligations as well as professional standards of clinical practice that underpin any actions taken to improve medication use. Professional standards are set by peers within professional groups and relate to:

- . the setting of guidelines for managing illness and health (usually framed by experts based on sound scientific evidence);
- . methods of clinical practice based on ethics and accumulated experience.

There are basic rights to information and a certain standard of management that are clearly stated. Legal protection through liability and other means exists, and the Trade Practices Commission and Bureau of Consumer Affairs continue to improve consumer protection. There are increasing calls from consumers for better quality communication with health professionals and more involvement in decision making.

Nature of the Problem

Improving the quality of medication use involves changing peoples' attitudes and behaviours and doing this within a health context i.e. writing prescriptions, ask questions, self-medicate, take anti-hypertensives regularly, choose a non-drug alternative, counsel patients etc. Therefore we need to look to the principles of health education/promotion and behaviour change for guidance, to help us identify effective tools.

Key Players

In order to move toward ideal medication use, there must be recognition of the interaction between the key players involved in medication use. These players, the pharmaceutical industry, health professionals, consumers and government must all work together if the goal is to be achieved.

Key Principles of Health Education

Health education uses the principles of behaviour change, adult education and incorporates techniques of diffusion and persuasion such as media advocacy and social marketing to assist individuals (collectively or separately) to make informed decisions about their own health or that of others.

Principles (cont.)

These principles have developed over the last thirty years and reflect the same rapid growth and development as the use of medication. Many theoretical models have been developed during this time and have been successfully applied to other public health areas such as smoking cessation, exercise and diet. However, whilst many argue the merits of one model over another, (eg. the Health Belief Model, Theory of Reasoned Action, Social Learning Theory, Multi-Attribute Theory etc.) current thinking is to integrate many of the key elements into an overall approach (for an overview of theories see Glanz et al 1990, Lee and Owen 1985, and Lefebvre and Flora 1988).

For example, Prochaska and Diclemente's model (1986) describes the stages that individuals go through in adopting a new behaviour or changing an old one, as well as providing information on the important elements for change between stages. Five basic stages are described:

- | | | |
|-----------------------------|---|-----------------|
| . Awareness of problem | } | Getting Started |
| . Motivation to change | } | |
| | | |
| . Taking up a new behaviour | } | Keeping Going |
| . Maintaining it | } | |
| . Dealing with setbacks | } | |
| and reversals | } | |

There is a continuum of attitudes, beliefs, knowledge, skills, motivation, information and resources needed, varying in emphasis, for individuals to move from one stage to another. People will obtain these in different ways, either on their own or as members of groups in the workplace, social settings etc., or from interacting with health and other professionals.

Another widely accepted fundamental principle is that the environment in which an individual or group operates has a significant impact on their desire and ability to change. Conversely, change at a personal level that is not reinforced or supported at other levels is difficult to sustain (Bandura, 1984).

Therefore, strategies to change behaviour need to be aimed at several levels simultaneously to maximise their chance of success. These levels are the personal, the interpersonal (eg. between patients and professionals) and the community/organisational level. Complementing these, and of equal importance, should be those aimed at the environmental/public health level, for example legislative or structural change (Winett et al 1989, Jeffery 1989, Ewart 1991).

Principles (cont.)

At the personal and interpersonal levels the approach of Prochaska and Diclemente is widely used to design education programs. Those involved in helping behaviour change identify the stage a person is at, for example in quitting smoking, and provide the person with the motivation, information and skills appropriate to move from one stage to the next. This requires skills in negotiation and motivation and the use of materials designed to reinforce the verbal messages. Alternatively, those who are motivated to do it on their own can work through a set of self-help materials.

In working at the group, community or organisation levels, principles of community empowerment are important (Minkler 1990, Glanz 1990). This involves building on or providing a sense of community competence, participation and ownership in programmes and 'starting where people are'. This is based on the concept that individuals must experience a felt need before they will learn or change. Therefore at this level, the community must identify needs and issues to be addressed. Ownership and participation are important to the success of efforts in change. These principles are mirrored in those of adult learning.

Useful health promotion planning models have been developed recently. The PRECEDE model was developed by Green (1980 & 1986). It provides a framework for identifying and analysing the changeable behavioural factors at the individual, group or community levels. Recent modifications add structural or non-behavioural factors to this model (Green & Kreuter 1991, PROCEED model, Hawe et al, 1991).

These models identify predisposing, enabling and reinforcing factors important in influencing individuals or groups to change. They are defined as follows:

Predisposing Factors: any characteristic of an individual, community or group that predisposes behaviour or other conditions related to health. This includes knowledge, belief and attitudes but may include other factors such as socio-economic status etc.

Examples: a lack of knowledge of appropriate prescribing/management guidelines predisposes to inappropriate or injudicious prescribing. Lack of belief that raised blood pressure has serious consequences predisposes to not taking hypertensive drugs and not adopting appropriate lifestyle change.

Enabling Factors: any characteristic of an individual, group or community that facilitates health behaviour or other conditions affecting health, including any skill or resource required to attain that condition.

Examples: the acquiring of skills to prescribe rationally within the context of the consultation during the undergraduate/postgraduate or continuing education. The availability of patient drug education materials.

Principles (cont.)

Reinforcing Factors: any rewards or punishment following or anticipated as a consequence of a health behaviour.

Examples: feedback from audit of prescribing habits, positive feedback from consumers, consumer satisfaction with professional interaction, control of disease, reversal of side effects.

Given the task of optimising the use of medicines in Australia involves a partnership between the major players, issues need to be defined from the perspectives of each. Strategies will be needed within groups and across groups in order to maximise change.

Analysis of problems at several levels will suggest interventions which will combine individual change strategies with system change strategies (Winett 1989). The result might involve a number of methods, settings and diverse personnel in an overall intervention.

In developing an overall framework for an education strategy to improve the quality of use of medicines in Australia, PHARM has identified three levels suitable for conceptualising and analysing problems:

Level One

This level encompasses awareness of medicines as a health issue. Community attitudes and beliefs about medicines are addressed as well as those of health professionals, industry and government to provide an environment conducive to optimal use of medicines. Awareness of the risk/benefit of medicines and knowledge of the full range of options for managing health and illness are key issues at this level.

Therefore, this level addresses all the elements that might be important prior to a situation where a decision to prescribe or self-medicate will be made, as well as ensuring a vigilant attitude in those already using medication.

Level Two

This level involves skills, knowledge and resources needed to make appropriate decisions at a personal and interpersonal level. It addresses issues important in deciding, prescribing and advising about medication in an informed way, aware of preventive options and choices for individuals.

Principles (cont.)

Level Three

This level deals with the knowledge, awareness and action needed to use medicines safely. It involves issues of monitoring of good and bad effects, quality assurance and problem solving.

An awareness that the audience for health educational messages will contain individuals at all levels is fundamental to planning. Messages can be designed for specific levels and appropriate outcome measures more accurately specified. For example, a campaign to raise the awareness of consumers (level one) might concentrate on explaining the benefits and risks associated with medication use, simple examples which forcefully put medication use of the agenda. Such a campaign could be evaluated by using indicators such as changes in knowledge, attitude, recognition of issues and familiarity with program themes.

The goal of optimising medication use in Australia is at once daunting, challenging and rewarding. Sub-optimal medication use has associated with it very large costs, both human and economic (Fryklof 1990). Indeed, for some groups such as the elderly, the consequences of sub-optimal medication use is seen as the most preventable cause of morbidity and mortality (Beers and Ouslander 1989). PHARM, in developing a conceptual and strategic framework from which to tackle problems of sub-optimal use and to ensure high quality use of medicines, has taken the first steps towards its goal.

REFERENCES

BANDURA, A. (1984) Self-Efficacy Mechanism in Human Agency, American Psychologist, Vol 37, pp 122-147

BEERS, M. & OUSLANDER J. (1989) Risk Factors in Geriatric Prescribing, Current Therapeutics, March, pp 107-112

EWART, C.K. (1991) Social Action Theory for a Public Health Psychology, American Psychologist, Vol 46 (9), pp 931-94.

FRYKLOF, L. (1989) Drug Cost Containment - The Case for Generics, Journal of Social and Administrative Pharmacy, Vol 6, p 1.

GLANZ, K., LEWIS F.M. & RIMER B.K. (1990) Health Behaviour and Health Education - Theory, Research and Practice, San Francisco, Jossey Bass.

GLANZ, K. (1990) Perspectives on Groups, Organisation and Community Interventions, in GLANZ K., LEWIS F.M. et al, ibid., pp 387-402.

GREEN, L.W. et al (1980) Health Education Planning - A Diagnostic Approach, Palo Alto, Mayfield Publishing.

GREEN, L.W. & ANDERSON C.L. (1986) Community Health, St Louis, Times Mirror/Mosby College Publishing.

GREEN, L.W. & KREUTER, M.W. (1991) Health Promotion Planning - An Educational and Environmental Approach, (2nd edition) Mountain View, Mayfield Publishing.

HAWES, P. et al. (1991) Evaluating Health Promotion, Sydney, MacLennan & Petty.

JEFFERY, R.W. (1989) Risk Behaviours and Health, American Psychologist, Vol 44 (9), pp 1194-1202.

LEE, C. & OWEN, N. (1985) Behaviourally-based Principles as Guidelines for Health Promotion, Community Health Studies, Vol IX, No 2, pp 131-138.

LeFEBVRE, R.V. & FLORA, J.A. (1988) Social Marketing and Public Health Intervention, Health Education Quarterly, Vol 115 (3), pp 299-315.

References (cont.)

MINKLER, M. (1990) Improving Health Through Community Organisation, in GLANZ K., LEWIS F.M. et al, op.cit., pp 257-287.

PROCHASKA, J.O. & DiCLEMENTE, C. (1986) Towards a Comprehensive Model of Change, in Treating Addictive Behaviours - Processes of Change, Miller W.R. & Heather N. (eds.), New York, Plenum Press, pp 3-27.

WINETT, R.Q., KING, A.C. & ALTMAN, D.G. (1989) Health Psychology and Public Health - An Integrative Approach, New York, Pergamon Press, pp 32-70.

Suggested Further Reading

MANASSE, H.R. Medication Use in an Imperfect World: Drug Misadventuring as an issue of Public Policy, American Journal of Hospital Pharmacy, Part 1, vol 46, May 1989 (pp 929-944) and Part 2, vol 46, June 1989, (pp 1141-1152).

Appendix IV: 'Why an Educational Strategy is Essential to the
Government's Rational Drug Use Policy',
Dr Andrea Mant

Why an educational strategy is essential to the
government's rational drug use policy

Over the past two years, the government has developed a statistical database on drug utilisation which has the cooperation of pharmacies throughout Australia and has the capacity to monitor the impact of government decisions, and to inform its advisory committees, specifically the PBAC.

The government has also funded independent research with very practical implications for drug use policy. An example is the project which demonstrated that removing the requirements for endoscopy prior to prescribing H₂ receptor antagonists such as ranitidine, cimetidine and famotidine was likely to be cost neutral. This project was funded through the PBSEP. The PBAC removed the requirement for endoscopy/radiology prior to prescribing H₂ RAs, leaving the government to negotiate the price.

The company which had most to gain in terms of market share from the regulatory change reduced its price below the \$30.00 Authority Cutoff (less than half the previous price). The other two companies' products are still "on authority", but their prices too are now much less (\$20.00 less) than was formerly the case. So the potential for savings to the tax payer on the annual expenditure of \$66.7mil (1990) for the drug group is there now. Of course, it could be offset if there is a large increase in prescription volume, because of the lack of an authority requirement. This is where education comes in.

When this extremely important decision was made, everyone was pleased: industry, general practitioners, pharmacists and consumers.

The only missing ingredient when the PBAC made its recent decision was the existence of an independent educational body with the resources and interest to ensure that the clinical discretion given to doctors would be exercised wisely. In the absence of such a body, the drug company with most to gain from the decision made a press release, organised a "roundtable" of experts to publicise the changes and to guide doctors on the importance of continuing to use endoscopy or radiology to confirm a diagnosis of peptic ulcer.

This is where PHARM's educational strategy can help in the future. Why leave it to industry to educate the profession? Why not establish an educational centre with the brief of informing the profession effectively. The very same body can and should tackle the task of keeping the public well-informed as well. This cannot be done through one-off projects. Rather, it needs a centre of excellence with an ongoing commitment for a minimum of five years.

